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(Succeeding Vol. 26, 1918, the Journal of Cutaneous Diseases)

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MARCH, 1923

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Archives of Dermatology and Syphilology

VOLUME 7 MARCH, 1923 NUMBER 3

CERTAIN DERMATOSES OF MONKEYS AND AN APE

PEMPHIGUS, SCABIES, SEBACEOUS CYST, LOCAL SUBCUTANEOUS EDEMA, BENIGN SUPERFICIAL BLASTOMYCOTIC DERMATOSIS AND TINEA CAPITIS AND CIRCINATA*

FRED D. WEIDMAN, M.D.

PHILADELPHIA

In recording these dermatologic states, I feel that a word of justification is appropriate, for, with only one minor exception, namely that of scabies, a knowledge of them can never be of any direct value in the practice of dermatology. The value of this knowledge lies in the relation of these conditions to the basic processes of dermatology; and involves that comparison of human diseases with those of the lower animals which is known as comparative pathology. The value of this line of attack on the hidden things of medicine is just becoming realized in general medicine, as is shown by the comparatively recent establishment of chairs of comparative pathology in some of our universities.

A comparison is made of the differences and similarities in the manifestation of a disease in several animal species. Then, by analyzing these data (preferably from a series of cases), and taking into consideration known differences in the anatomies, the physiologic condition and bionomics of the animals, more or less definite deductions may be made, which I cannot go into here, and which cannot be set down until the case in point occurs.

The value of these animal cases varies. With some it amounts to no more than that a certain condition occurs in animals just as it does in human beings, and isolated cases of this kind are of only passing interest. With an accumulation of such occurrences, however (to the exclusion of related processes in human beings, for instance), their value rises, and they are therefore included in this series.

* From the Laboratory of Comparative Pathology, Philadelphia Zoological Gardens, and the Laboratory of Dermatological Research, Department of Cutaneous Medicine, University of Pennsylvania.

PEMPHIGUS IN THE ORANG-UTAN

The first of these dermatoses that I saw was an attack of pemphigus in an orang-utan, of which a report has already been printed.[1] Therefore I shall give only an abstract of the case. To our knowledge, the disease had lasted for about eighteen months, during which time there had been perhaps a dozen outbreaks, with brief remissions. The blebs occurred in groups, affected alike the extremities and the trunk, which never itched. The blister fluid was somewhat turbid and contained a large proportion of eosinophils. In summarizing this article, I said: "The case presents nothing unusual in the symptomology of pemphigus but is made reportable because it occurred in a lower animal and because it was associated with intestinal worms and was terminated by tuberculosis. The last two features are here recorded for what they are worth, without speculation by the writer. Future findings only will show whether they played any part in the etiology of the disease; but knowing what large numbers of pemphigus-free monkeys have died in the gardens of tuberculosis, and that, on the other hand, worm-infested Johanna (the cagemate of this orang-utan) has never shown cutaneous disturbances of any sort, we can state that their effect, if any, is only on especially susceptible individuals with lesions or functions disturbed in a way more or less nicely adapted and within narrower or broader bounds to produce the special lesion in the skin."

SCABIES IN THE ORANG-UTAN

My report concerns a young animal whose age was estimated at 3 years, and which had just arrived in the Gardens. Its skin from the very first was very harsh over the extensor surfaces and over the scalp, and was elevated into papillary eminences around the roots of the hair follicles as in keratosis pilaris. The animal scratched itself continually, particularly over the back; and as a result the lower dorsal parts, extending almost to the anus, were largely bare. No lesions could be discovered between the fingers or over the ventral portions of the body to confirm the suspicion of scabies. In fact, the venter was much more free from signs of disturbance than the dorsal parts.

The only isolated skin lesions which could be discovered, even on examination under the lens, were three or four patches on the back, the largest 4 or 5 mm. in diameter, which looked like small, scaly, elevated patches of eczema. I could find no burrows. There were one or two smaller patches on the scalp, certainly not more than 2 or 3 mm. in diameter. Scrapings from these patches were examined in sodium

1. Weidman, F. D.: Pemphigus in an Orang-utan, Jour. Cutan. Dis. **37**: 169 (March) 1919.

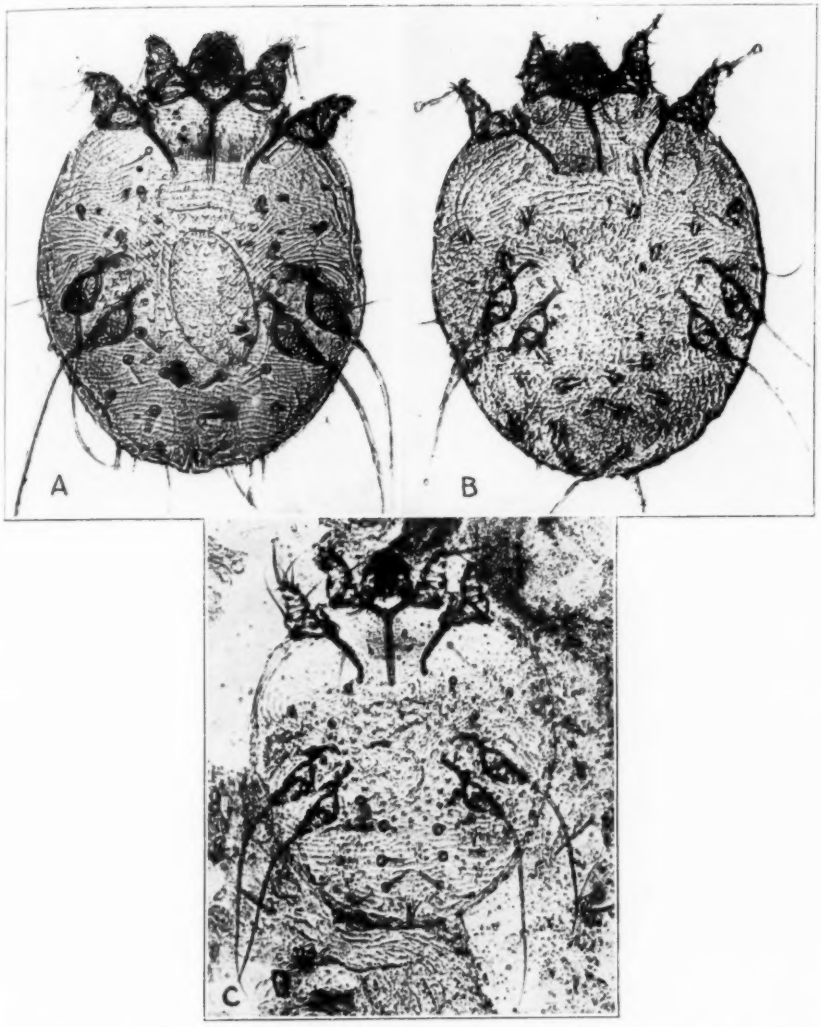

Fig. 1.—*A* and *B* are photomicographs of human specimens and *C* is that of the orang-utan, at the same magnification. *B*, in passing, has the ovum at the anterior end, which is a most unusual position. The outline of the ovum is poor in this illustration because the mite could not be sufficiently flattened to bring it into the same focal plane as the cuticle.

hydroxid solution. In one preparation only were parasitic forms discovered, consisting of ova and a solitary itch mite, as shown in the photomicrographs.

The Orang-Utan Mite.—Flattened out under the coverglass after two weeks in 10 per cent. sodium hydroxid solution, it measured 0.40 mm. long and 0.32 mm. wide, and was of the same general broadly oval form as the human species. The structure of the head agrees with Fürstenberg's [2] original figure of the human variety, except that he represents four pincers (chelicers). This may have been a mistake on his part, for Megnin [3] (a later worker) could make out only two, so that we may reasonably assume that the head of this orang-utan specimen has the same architecture as the human variety. Likewise,

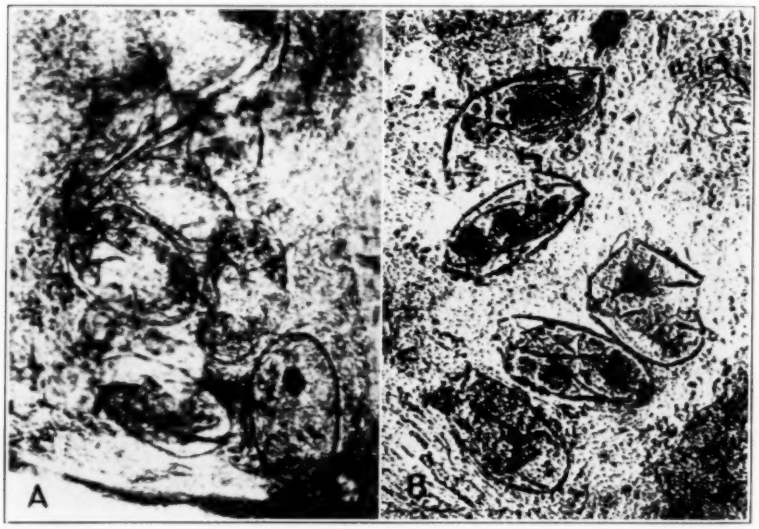

Fig. 2.—*A*, ova of human species: *B*, ova of the orang-utan. The illustration shows the size of both, but not the form, as the ova of the orang-utan are empty and have collapsed. (The outline of the larva can be traced in one of the human ones.)

there was no disagreement with the human species as to the structure of the legs and the position of the anus and vulva.

In fact, the only features of this orang-utan specimen which could have any possible bearing in indicating a new orang-utan species were the cutaneous appendages, such as spines and hairs, and I will not describe these because their numbers and positions are about the same

2. Fürstenberg, M. F. H.: Die Kratzmilbe der Menschen und Thiere, Leibzig, Wilhelm Englemann, 1861.

3. Megnin: Les Parasites Articules, Paris, G. Masson, 1895.

as in the human species, and they are better brought out in the illustrations. But it is necessary to indicate certain differences in form, etc., from the human. These are not important, being for the most part but relative differences, and they might be nonvalid if I had had larger numbers of orang-utan mites from which to construct a general picture. I do not wish to emphasize them—only to mention them. The "differences" between this one orang-utan mite and the (fifty) human ones which I studied in Philadelphia are:

1. This orang-utan specimen lacks the pair of minute chitinous "runways" immediately at the vulvar orifice, which is designed (Megnin) in the human variety to expedite the escape of the ovum.

2. The dorsal spines of the orang-utan mite are not as sharp.

3. The six dorsothoracic spurs are half as long as those of the human variety.

4. The pair of hairs at the nape of the neck (orang-utan specimen) could not be made out. This may have been due (unless they were

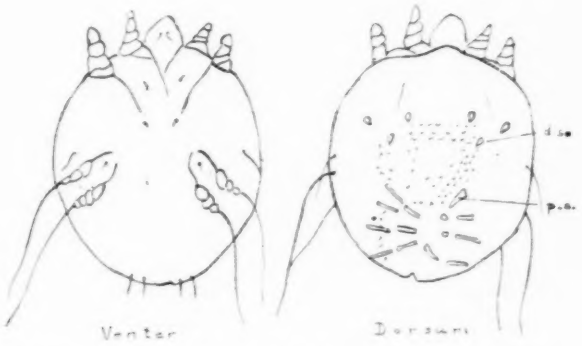

Fig. 3.—Camera lucida drawings showing details of cutaneous appendages: *d.s.*, dorsal spines (6); *p.s.*, preanal spines (14).

actually absent) to obscuration by the mass of overlying mouth parts, since the specimen could be viewed ventrally only. (The mite was softened by the sodium hydroxid solution to the degree that it could not be turned over).

5. The fourteen preanal spurs (orang-utan specimen) are extremely blunt. They look "chopped off."

Determination of Species.—Was this orang-utan specimen one of the human variety, or was it like one of those occurring on the lower animals? There was a bare possibility that the animal might have contracted the disease from a horse blanket of which she was very fond, and the equine variety has therefore been strongly suspected. Accordingly, the mite and the ova were photographed, measured and compared with actual human examples and with published data of the several animal species.

In this comparison it was eventually found necessary to consider all the known species of *Sarcoptes* because the orang-utan might have been exposed to infestation from a variety of animals while in the hands of keepers and dealers before she reached us. Canestrini and Kramer [4] list fourteen species as valid and four as questionable. They were found on such different animals as the horse, dog, dromedary and lion,[5] nineteen different animals in all. Other authorities do not agree that these are all separate species, and leave much to be desired in the way of a basis for settling the standing of the orang-utan mite.

It would be tiresome to recount here all the considerations involved in finally arriving at the taxonomic conclusion. In brief, both as to my human and orang-utan specimens, I do not believe that such a conclusion could at present be arrived at from the strict zoologic standpoint without making a laborious comparison first-hand of the several animal species. After studying my fifty human specimens and the data in the literature, I feel that in the absence of breeding experiments there are too many sources of error contingent on individual variation and the effect of environment to enable one to draw any conclusions on a purely morphologic basis.

But one factor in the determination of species which I wish to speak of particularly here is that of size. Considerable latitude in one and the same species must be allowed in this respect, and the technic of examination specified. The human mites I studied were mounted (and flattened) in liquor formaldehydi under coverslips. Measured thus, of fifty specimens examined, the largest mature specimen measured 0.572 by 0.442 mm. and the smallest 0.337 by 0.324 mm. Furthermore, size varies according to the degree of coverslip pressure. Thus, a mite photographed under a coverslip in an abundance of water measured 0.375 by 0.250 mm. With the water largely evaporated and the parasite flattened, it measured 0.433 by 0.335 mm.—an increase of about 14 per cent. in length and 20 per cent. in width. The ova behaved similarly, increasing 12.6 per cent. in length and 15.4 per cent. in width.[6]

The strict zoologic relation between the orang-utan and human species has not been established. This is not true medically, for there are numerous individuals among my fifty human mites which would vary morphologically just as widely from the remainder as did the

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4. Canestrini and Kramer: Demodecidae und Sarcoptidae das Thierreich, Deutsch. Zool. Gesellsch. Berlin, R. Friedlander u. Sohn **50**:7, 1899.

5. Fantham, Stevens and Theobald: Animal Parasites of Man, New York, William Wood & Co., 1916, p. 520.

6. Weidman, F. D.: Variation of the Ovum (Sarcoptes scabiei) Under Coverglass Pressure, J. Parasitol. **6**:155 (March) 1920.

orang-utan specimen, yet which obviously had the capacity to produce human disease. The deciding argument from the practical medical standpoint was the further course of events. The beast's keeper later developed a severe case of typical scabies (wrists, hands, abdomen, chest and thighs), which cleared up under treatment with sulphur ointment; and shortly thereafter the keeper's wife had the same experience. There were no burrows on the keeper's skin, and I was not successful, as usual, in teasing any mites from the papules.

Scabies evidently occurs rarely on monkeys. Toomey,[7] in his recent comprehensive survey of animal scabies in relation to man, mentions no cases other than mine. Fürstenberg [8] reports that the human variety has been found in monkeys, but does not describe the parasite or give the original reference. The other authors—Megnin, and Canestrini and Kramer do not mention the occurrence of the parasite on monkeys or apes. The subject was beyond the scope of Heller's [9] compilation of animal dermatoses.

From the general pathologic standpoint, we are fortunate in this ape case in having been able to work with the definite etiologic agent—a desideratum generally either absent in work in comparative pathology or so uncertain as to compromise its usefulness. But in this scabies case our good fortune enables us to declare that the differences between the skin of the orang-utan and human skin were sufficient to bring about a difference in the distribution and character of scabies lesions, for they were produced by the same agent. It would seem at first that a comparison and analysis of the distribution of the lesions and of the anatomy and physiology of the skins of the two hosts would lead to an explanation of the special distribution of human lesions, but I have not been able to devise one.

Summary.—An attack of scabies in an orang-utan which did not conform to human scabies in lesion or distribution is described. The single mite found may be accepted as identical with the human form in view of its morphology and the transmission of the disease to the orang-utan's keeper. The latter phase of the case should be kept in mind when dealing with scabetic persons who have pet monkeys.

PILOSEBACEOUS CYSTS IN RHESUS MACAQUE

Cysts occurred on the lids and brows of a young macaque (estimated as being 4 years old) following an injection of epithelioma contagiosum virus of birds. The latter procedure had no significance, however,

7. Toomey, N.: Urol. & Cutan. Rev. **26**:473 (Aug.) 1921.

8. Fürstenberg: Die Kratzmilbe der Menschen und Thiere, p. 209.

9. Heller, J.: Vergleichende Pathologie der Haut, Berlin, Aug. Hirschwald, 1910, p. 279.

since the virus had been rubbed into the lower lid, whereas these lesions occurred only on the upper lid and on the eyebrow. Moreover, the virus had been rubbed into the eyelids of four different monkeys, and in only one did these cysts develop.

There were at first six closely-placed, miliary, yellowish-white nodules located on the right upper eyelid fairly close to the inner canthus but well above its ciliary margin. They were tense, yellowish-white, not umbilicated, and projected high above the skin surface after the fashion of molluscum contagiosum lesions. They persisted for eight weeks and showed no signs of regression at the time the animal was killed in other work. A few smaller, slightly elevated and poorly

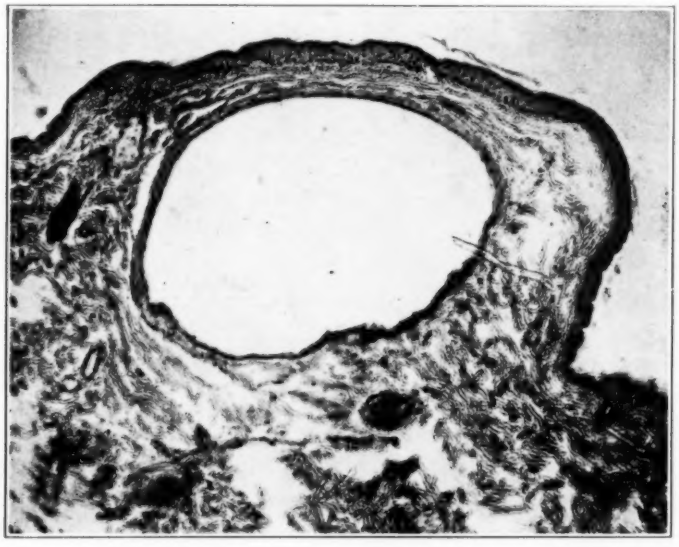

Fig. 4.—Sebaceous cyst; low power photomicrograph.

developed nodules appeared later on the left eyebrow; one of these was excised and examined microscopically.

Histologic Study.—There is nothing resembling molluscum contagiosum in the illustrations; the essential lesion is a simple cyst lying in the corium. Examination did not reveal anything abnormal in the epiderm or in the corium, with the exception of the cyst. Several small sebaceous glands were noted, but none in immediate relation to the cyst. The cyst was lined by three or four layers of flattened squamous epithelium, the more interior ones of which contained coarse blue granules (hematoxylin and eosin sections) similar to those in the stratum granulosum of normal skin. There were no villous projections. The contents had escaped from paraffin sections, but were

observed in frozen sections, and comprised epithelial scales, fatty detritus and a few segments of lanugo hairs. There was no evidence of frank inflammation as in a folliculitis.

It is not necessary to discuss here the more minute classification of dermal cysts as set forth by Aschoff [10] and Chiari,[11] and more recently by Sherk.[12] The presence of the stratum granulosum cells in the lining permits its inclusion among the sebaceous cysts, and the presence of hairs exclude the epidermoid (miscalled dermoid) cysts.

BANDLIKE EDEMA OF THIGHS IN MENSTRUATING MONKEY (RHESUS MACAQUE)

This monkey has been under my observation for five years. Four years ago, we began to mix solution of potassium arsenite (Fowler's

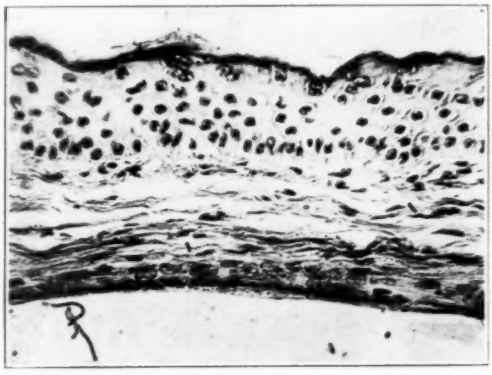

Fig. 5.—Portion of "roof" of sebaceous cyst; epiderm above and cyst lining below; eleidin granules in the latter.

solution), three drops three times a day, in her food in an attempt to induce arsenical hyperkeratoses. This medication was continued for six months, and altogether she received 4½ ounces (139.9 gm.) of the solution. While midway in the treatment, we noticed that when she was menstruating a heavy band of subcutaneous edema sometimes extended from the hips downward, and that it subsided, sometimes disappearing, as menstruation ceased. This phenomenon was not observed at every menstrual period. It has occurred two or three times each year for the last three years.

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10. Aschoff, in Lubarsch and Ostertag: Ergebn. d. allg. Path. u. path. Anat., 1895, p. 471.

11. Chiari: Ztschr. f. Heilk. **12**:189, 1891.

12. Sherk, H. H.: Epidermoid Cysts, Surg., Gynec. & Obst. **33**:494 (Nov.) 1921.

In its most marked expression the lesion extended from the crest of the ilium downward over the lateral aspect of the thighs and backward over the popliteal space, where it became narrower, and then continued over the calf and tapered down to the ankle. In width the band varied between 1.5 and 2 cm. It was elevated fully 4 or 5 mm. above the general surface, and its margins were rounded. Its surface was depressed by transverse furrows at various intervals through its whole course from the hip to the ankle, which thus divided it off into shorter and longer segments, and gave it a lumpy character. The overlying skin had the normal bluish-gray shade of monkey skin—that is, there was no hyperemia or other evidence of inflammation. At other times, the band would shift to a more posterior position and be less highly developed, as shown in the illustration. The band must have

Fig. 6.—An edematous cord extending down the back of a lower extremity. The animal is being held face downward. There is so much fluid in the "cord" that it sags.

contained a clear, watery interstitial fluid. Pressure could easily reduce the skin to almost normal thickness. The band was not due to urticaria, for there were no signs of itching, nor was it a wheal, for the fluid evidently lay in the subcutaneous parts. After it had receded with the cessation of menstruation the overlying skin remained slightly folded for a few days as though it had not quite recovered from being stretched. There was no resultant fibrosis—even after a dozen or more attacks.

So far as I have been able to learn, the presence of such a band is a rarity, if not indeed unique, at any time. The keeper at the Philadelphia Zoological Gardens says that he has never noticed it in any of the animals under his care.

This phenomenon is interesting in connection with monkey menstruation itself. It is common knowledge that the buttocks and external genitalia of the females of several species of monkeys (including *Rhesus*, especially, and the baboons) normally become extremely reddened and swollen during the molimen.

A third menstrual condition is that of the face. In some females it is normally never red, while in others of the same species it is naturally red at all times; some pale-faced monkeys become red during menstruation, and red-faced ones become more so. This condition corresponds to acne rosacea and acne vulgaris in human dermatology, which become worse in females during the molimen. We have a striking example in this monkey of the connection between the visceral phenomena and alterations in the skin exemplified in two cutaneous processes—edema and erythema. The facial erythema suggests a phylogenetic explanation for the human acne exacerbations, involving at least a latent reflex nervous pathway for the vessels of the face and the nervous tracts concerned during menstruation.

The constancy and consistency with which this cordlike or bandlike edema occurred perplexes as well as interests us. I never saw it otherwise, that is, it never occurred diffusely in this animal. In searching for an explanation, the mind naturally turns to the influence of some anatomic structure which extends lengthwise down the lower extremities. The clinical appearance of this monkey showed that there was no disturbance of the blood vessels. The anatomy of the lymphatic spaces is too uncertain to allow even the promise of profitable speculation. Only the nerves are left, and we recall the linear nevi, zoster, etc., but in the absence of further data, we can have only a strong suspicion that nervous stimuli, reflex from reproductive (or other) nervous tracts, may excite an edematous process in the subcutis quite apart from any circulatory factor and therefore through metabolic agencies. Looking at it another way, the edema in this monkey case reflects the metabolic perversion of tissue cells which are under the influence of abnormal nervous stimuli. From this it is but a step farther to our more or less accepted conception of the pathogenesis of certain noninflammatory dermatoses (the atrophies for instance) in which there is already the clinical suspicion of a nervous basis, but not the linear architecture to more or less clinch it.

It must be conceded that there may be an arsenical factor in this case, but there were no clinical evidences of neuritis, no palsies, and no albumin or casts in the urine. Arsenicism may well be playing a part in determining the edema and its linear distribution, but even granting this, it would not militate against the value of the menstrual cyclic phases of the case.

BENIGN SUPERFICIAL BLASTOMYCOTIC DERMATOSIS OF THE AXILLA OF A MONKEY

A *Rhesus macaque,* which was sacrificed at the Zoological Garden as a tuberculosis suspect, but whose emaciation was found to be due instead to chronic suppurative perio-ophoritis, had a thick scaly surface deposit more or less entangled in the hair, which could have passed for "dandruff," except for its pale but distinctly lemon yellow color. At necropsy, it was considered as seborrhea. It affected both axillae, extended well down the sides of the chest, and gradually faded out into the surrounding sound skin. In other body parts, the skin was normal, except for some dandruff-like scales lying loosely in the hair of the back. The scalp appeared normal.

Fig. 7.—Scrapings from axilla containing double-contoured yeast cells.

Extemporaneous sodium hydroxid preparations of the axillary scales showed cornified epithelium interspersed with great masses of double-contoured spores, which collectively transmitted to the eye a distinct yellow tint; they were present in such quantities as to be easily responsible for the yellow tint seen clinically. Individual spores were of the same type as those of *Microsporon furfur*—double-contoured and with refractile hyaloid centers—but they were much larger, were collected into larger groups, and were unassociated with mycelium.

Cultures did not yield hyphomycetes. Besides various bacterial colonies, two kinds of blastomycetes developed. The first appeared as only one colony, grew rapidly and microscopically suggested a cryptococcus. It has not been regarded seriously as the valid organism of the disease, because it developed so sparingly (in spite of being a free-

grower) from original material that reeked with the cells, and for additional reasons that will be given later.

The second yeast was at first only observed intermixed as part of bacterial colonies from which I was never able to isolate it; but finally some pure colonies became visible. The latter, even when four weeks old were so small as to be invisible to the naked eye. They were detected only after three weeks during a microscopic survey of a petri dish planting; obviously this organism is a very weak grower. The colonies were round and colorless and homogeneous.

I have made repeated efforts to obtain subcultures from the originals, but without success. Thus, while still under the microscope, fishings have been made from them and transferred variously to glucose bouillon tubes, to glucose agar in tubes and plates, and to hanging-drop preparations (glucose bouillon). A "hanging-drop block" has been made by (microscopically) cutting colonies from the original plate and transferring them to the microscopic moist chamber. They have been kept both at room temperature and at 31 C. But under this new environment—one which is almost perfect—not one of the cells has been observed to bud.

All this means that this yeast grows best on glucose agar; but it grows feebly and only up to a certain point or for a certain time. At the same time, it is disconcerting that none of the cells has passed into the resting stage ("durable cells" of Guilliermond), which should be expected if their environment is unsuitable, and in view of the "durable cell" type observed in the extemporaneous sodium hydroxid preparations.

At this point it must be noted that this "feeble grower" was the only yeast observed among the original scales after they had been lying on glucose agar for two weeks. At this time, the larger part of the scale was covered with a deep yellow bacterial growth, while the remainder was gray-white; it was in this gray-white part that the feeble grower occurred pure or intermixed with smaller masses of bacterial forms. Here the double-contoured bodies originally seen had disappeared and must have developed into budding forms. This observation is important with the evidence already cited that the feeble grower is the one developing from the original double-contoured "spores" and not the free-grower.

Individual yeast cells from these weakly growing colonies are distinctive as pathogenic yeasts go. First, they are small. The largest forms measure 0.005 by 0.002 mm. and the smallest are scarcely distinguishable from bacilli, measuring only 0.003 mm. in length, and being from a third to a quarter as wide. Second, their form is not always the usual spheroid or ovoid one. Only larger forms are ovoid, and these may be apiculate at one end and contain a few small granules and occasionally a minute vacuole. Intermediate sized cells contain

no granules or vacuoles. They occur frequently in pairs, as though in process of transverse fission. Often a barely visible bud may be seen projecting from the point of separation; and more uncommonly, such a bud is seen on either side of this point. The smallest forms are elongated—fully four or five times as long as they are wide—have rounded ends, and are frequently more or less loosely joined in pairs, apparently undergoing transverse fission (*Schizosaccharomyces*). They might thus be mistaken for large bacilli but for the less opaque appearance of their substance and their more uneven sides. Mycelial forms, ascus formation or double-contoured cells have not been seen.

Histologic sections of axillary skin added nothing to our knowledge. Most of the surface scale was lost during the histologic process, and that which remained showed none of the organisms. There was not the slightest trace of epidermal hyperplasia, inflammation of the corium, or alteration of the sebaceous glands. A certain grade of capillary hyperplasia in the deepest part of the corium, attended by swelling of the lining endothelial cells, may have been due to the peregrinations of filariae with which the animal was infested.

This was evidently a harmless affection akin to the human tinea versicolor, but differing in location, color and causative organism. At most, it can be said that clinically it induced only a mild grade of surface hyperplasia.

I have been constrained to use a cumbersome title. Thus, the idea extant of blastomycosis is that it is deep-seated and must be a serious affection. The disease was not related to the hairs—it was not a trichomycosis. It was not inflammatory and not a dermatitis. I have already differentiated it from tinea versicolor. Biologically, it is the harmless, superficial, commensal condition which the title indicates. As a comparison with human disease, the case is pertinent only in that it is somewhat analogous in its pathology to human tinea versicolor, and in that a description is given of a micro-organism from a monkey which might some day be matched by one obtained from human sources.[13]

13. As this goes to press an instance of ringworm in two young Barbary apes comes to hand. One died, and necropsy showed three rings of scaliness over the left side of the abdomen, the centers of which were hairless. There were two or three smaller, solid patches also present farther around on the loins, which appeared seborrheic. In extemporaneous sodium hydroxid preparations a coarse, rarely-branching mycelium was found ramifying through the thickened follicle sheaths—not in the substance of the hair itself. The mycelium had a pale but definite brick-red color such as I have never seen before, and the metachromatic granules in the interior of the segments were much more strongly colored than the fungicellulose elsewhere. Cultures have just been started, and results therefrom will be reported later. The second animal is even more extensively affected, still alive and well, and has patches on the scalp as well as on the abdomen and flexor surfaces of the extremities where the hair is thin.

GRANULOMA INGUINALE *

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NEW ORLEANS

"In 1882, Colonel Macleod,[1] in India, described a serpiginous ulceration of the genitals, probably the first case noted. In 1896, Conyers [1] and Daniels,[1] in British Guiana, adequately described and defined it as a clinical entity and gave it the name of granuloma inguinale tropicum. In 1897, Galloway [1] added observations, and called the condition ulcerating granuloma of the pudenda. Cases have since been reported in Brazil, West Indian Islands, West Africa, Tripoli, South China, North Australia, New Guinea, and the South Sea Islands." Cases have been reported in different parts of the United States and dependencies by Goodman,[2] in Porto Rico, four cases; Pederson,[3] in St. Thomas, Virgin Islands, three cases; Geringer,[3] in Panama, one case; Pardo,[3] in Cuba, two cases; Grindon,[4] in St. Louis, three cases; Symmers and Frost,[5] in New York, two cases; Campbell,[6] in New York, three cases; Jessup,[7] in New York, one case; Reed and Wolf,[8] in New Orleans, five cases; Lynch,[9] in Charleston, S. C., nine cases; A. Randall, J. C. Small and W. P. Belk,[10] in Philadelphia, eleven cases of their own, with four other cited cases, and Clyde F. Ross,[11] in

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* From the Outpatient Department, Surgical Clinic. Touro Infirmary.

1. Quoted by E. L. Walker: The Etiology of Granuloma Inguinale, J. M. Res. **37**:427 (Jan., 1918).

2. Goodman, Hermann: Ulcerating Granuloma of the Pudenda, Arch. Dermat. & Syph. **1**:151 (Feb.) 1920.

3. Quoted by Goodman: Ulcerating Granuloma of the Pudenda, Arch. Dermat. & Syph. **1**:151 (Feb.) 1920.

4. Grindon, G.: Granuloma Inguinale Tropicum, J. Cutan. Dis. **31**:237 1913.

5. Symmers, Donald, and Frost, A. D.: Granuloma Inguinale in the United States, J. A. M. A. **74**:1304 (May 8) 1920.

6. Campbell, M. F.: Granuloma Inguinale, J. A. M. A. **76**:648 (March 5) 1921.

7. Quoted by Campbell, Footnote 6.

8. Reed and Wolf: Treatment of Granuloma Inguinale, with Exhibit of Cases, New Orleans M. & S. J. **74**:25 (July) 1921.

9. Lynch, K. M.: Granuloma Inguinale, J. A. M. A. **77**:925 (Sept. 17) 1921.

10. Randall, A., Small, J. C., and Belk, W. P.: Tropical Inguinal Granuloma in the Eastern United States, J. Urology **5**:539 (June) 1921. Randall, Small and Belk report sixteen more cases from Philadelphia, Surg. Gynec. & Obst. **34**:717-739 (June) 1922. This makes a total of seventy-five cases reported in the United State and dependencies.

11. Ross, C. F.: Granuloma Inguinale, Virginia M. Monthly **48**:579 (Jan.) 1922.

Richmond, Va., seven cases. This makes a total of fifty-five cases reported in the United States and dependencies, to which I shall add four cases.

ETIOLOGY

"Conyers [1] and Daniels [1] (1896), Le Dontic [1] (1900) and Jeonselme [1] (1904) considered the disease a tuberculous infection. Le Dontic claims to have produced tuberculous lesions in animals by inoculating them with material obtained from granuloma inguinale.

"Wise [1] (1906), Maitland [1] (1906), and Bosonquet [1] (1910), found spirochetes of the treponema type in the lesions, and these authors believed granuloma inguinale to be a manifestation of syphilis. Plehn [1] (1914) said that he could see no reason for separating granuloma inguinale from phagadenic chancres of extratropical regions. MacLennon [1] (1906) observed *Spirochete refringens* in the lesion. Cleland [1] (1909) found a spirochete in a case of granuloma inguinale in a native of Australia, which he named *Spirochaeta aboriginalis*, which he considered the cause of the disease.

"In 1905, Donovan [1] observed cell inclusions in granuloma inguinale, which have since been found in the mononuclear cells (endothelial leukocytes) of the lesion. Donovan considered these inclusions development stages of a gregarine. Carter [1] (1910) looked on them as a gregarine type of a crithidia or herpetamonad. Flu [1] (1911) thinks that the reaction of the infected cells in granuloma inguinale is suggestive of the chlomydoza.

"Seibert [1] (1907) and Martini [1] (1913) identified the intracellular organisms as encapsulated diplococci. Martini was able to obtain the organisms in pure culture, and he produced local abscesses by subcutaneous inoculation which the author considered comparable with granuloma inguinale.

"Flu [1] (1911) suggested that this intracellular organism of granuloma inguinale might belong to the group of capsulated bacilli. This author obtained a gram-negative, nonmotile, capsulated bacillus in culture from the lesion of a case of granuloma inguinale. In a second culture he obtained a gram-negative motile bacillus, and in view of these diverse results, he considered his results doubtful.

"Aragão and Vianna [1] (1913) found the intracellular organisms constantly in cases of granuloma inguinale in Brazil. These authors obtained in pure culture an organism having the same morphological characteristics as those observed in the lesion. They considered the organism to be a schizomycete, but to constitute a new genus, which they designated as Calymmatobacterium, and named the specific organism *Calymmatobacterium granulomatis*. Aragão [12] (1917) reaffirms the

12. Aragão, H. de B.: Notes on Granuloma Venerium, New Orleans M. & S. J. **24**:369, 1913.

claims of *Calymmatobacterium* as a distinct group of schizomycetes, to which the organism of granuloma inguinale belongs."

E. L. Walker [13] (1916) observed a case of granuloma inguinale in a Madeira-Marmore railway hospital, Porto Velho Amazonas, Brazil. He was able to demonstrate the capsulated organisms in the cytoplasm of the large mononuclear cells, of which several types could be distinguished. He considers the zoogleic masses noncapsulated rods, and rounded bodies to be development stages of the organism. He also found the *Spirochcta refringens* type in the smears.

Walker was able to obtain in pure culture, in all types of culture mediums, a gram-negative, nonmotile bacillus (short plump rods, often coccobacilli) that showed a definite capsule. He classified the organism that he isolated with the so-called capsule bacilli of which *Bacillus mucosus-capsulatus* of Friedländer is the type. He injected pure cultures of the organism subcutaneously in laboratory animals and was able to produce lesions that were comparable to those of granuloma. The lesions usually healed in from two to four weeks and showed no evidence of chronicity, which is so characteristic of the disease. He also inoculated a monkey and two male negroes, with negative results. Randall, Small and Belk [10] of Philadelphia, also Lynch [9] of Charleston, S. C., have corroborated Walker's work. However, they did not express an opinion as to the type of organism.

One can see from the foregoing the diversity of opinion that exists as to the etiologic factor of the disease.

Since granuloma inguinale was first described, three questions have engaged the investigators in this field and are as yet unanswered: 1. Is the disease a primary infection or is it a low grade secondary infection superimposed on a primary venereal infection? I believe that the majority of cases, if not all of them, are a primary infection of the external genitals, usually transmitted through sexual intercourse. However, the disease may be complicated by either chancroid or syphilitic infection, as shown by case reports in the literature. 2. Is the specific organism, whether it be a primary invader or not, the encapsulated organism decribed by Donovan? This organism, which has been demonstrated in lesions of granuloma inguinale by writers throughout the world, and which presents a definite and uniform morphology in all cases, having the same relationship to the endothelial leukocytes and their distribution in the tissue, seems to me to be the most probable cause of the disease. However, it may owe its foothold in the tissue to some other organism or organisms, as yet undetermined, acting in symbiosis with the organisms described by Donovan. 3. Is the organism

13. Walker, E. L., The Etiology of Granuloma Inguinale, J. M. Res. **37**: 427 (Jan.) 1918.

of the vegetable or the protozoan type? Its similarity clinically to other types of protozoan diseases, its marked chronicity, and prevalence in tropical and subtropical countries, and its quick response to tartar emetic medication, which has been heretofore most efficacious in diseases of the protozoan type, suggest that it bears a close relationship to the protozoan group. Although the organisms that have been cultured from the lesions conform to the bacterial group, and although lesions have been produced in laboratory animals that simulate the true lesions of granuloma inguinale, these lesions have not shown the chronicity of the lesions that occur in the human race.

BACTERIOLOGY AND PATHOLOGY

Smears were obtained from the lesions by means of the curet, the lesion having previously been cleansed with ether. This method of obtaining smears is not to be recommended, as too much blood is obtained, diluting the material, and fewer organisms are obtained. The best method is to take out a section of tissue and squeeze out the tissue fluid, making smears from this. Another satisfactory method is to clean the ulceration thoroughly, and if bleeding occurs, use pressure until it is stopped. Then, with a swab or knife, the surface should be scraped very gently and smears made from the scrapings. By this procedure, almost pure smears of the organisms can be obtained.

The smears were stained with Wright's stain, which gave very satisfactory results, the organisms showing a dark blue or red stain for the chromatin and a pale blue or pink stain for the cytoplasm or capsule.

The organisms were found in the cytoplasm of the endothelial leukocyte, while in some smears they are found free from the cells. They show different shapes and sizes in the same smear, which I consider development stages. Some of the endothelial cells contain only a few organisms (Fig. 5), while others are filled to bursting. The organisms are usually situated near the nucleus of the cell when they are in small numbers; and when in abundance they practically occupy the entire cytoplasm. Some of the endothelial cells show a vacuole in the cytoplasm, which contains large numbers; while others show partial or complete destruction of the endothelial cell by the organisms. Then again we see the endothelial cell overcoming the organisms by phagocytosis.

All types of bacteria, débris and blood cells can be found in the endothelial cells, which are great phagocytes, so one must be careful in drawing conclusions as to the presence of the Donovan bodies.

I have found the following types of organisms in the smears: (*a*) zoogleic masses containing single dots of chromatin; (*b*) bipolar

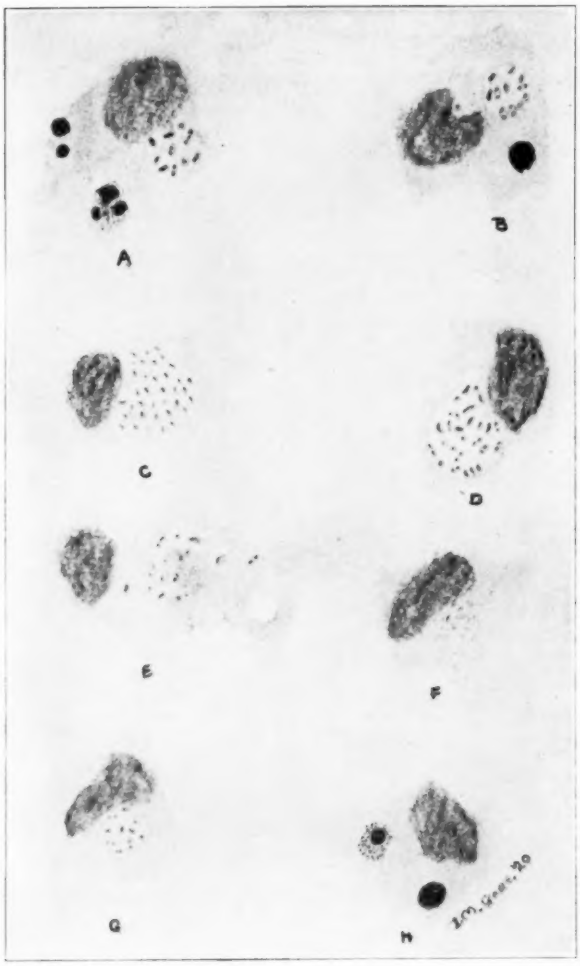

Fig. 1.—Drawings made from a smear obtained from a case of granuloma inguinale, and stained by Wright's stain. (Oil immersion; not drawn to scale.) *A*, *B*, *E* and *G* show typical types of the organisms as found in the endothelial leukocytes: coccoid, bipolar (occurring in the form of coccoid and short rods), short rods and long rods somewhat curved. All the organisms show a definite capsule and seem to occur in a vacuole in the cytoplasm of the endothelial leukocyte. *E* shows for the most part organisms that are of the coccoid type, while some of the capsules or cytoplasm is void of organisms or chromatin. *A*, *B* and *H* show erythrocyte, lymphocyte and eosinophil contained in the cytoplasm of the endothelial leukocyte. *C* and *F* show organisms that have lost most of their characteristics in that they do not show a definite capsule, most marked in *F*. It is most probable that here the organisms are being phagocytized by the endothelial leukocyte.

organisms; (*c*) organisms presenting two short rods at each end; (*d*) long rods, some of them being curved. These different types can be seen in Figure 7. Not all of the organisms contained a capsule or cytoplasm. Some of the bipolar types show a constriction between the two dots of chromatin, which appears to be a division of the organism. Spirochetes of the refringens type were found in Case 2, but were few in number.

Fig. 2. (E. R., negro).—Typical lesions of granuloma inguinale around stump of penis (amputated), scrotum and inguinale region, with secondary lesions on thigh and at site of old suprapubic wound; elephantiasis of scrotum.

Cultures from the cases have been very disappointing. A gram-negative and gram-positive encapsulated organism has been obtained by culture. The culture from the first case was contaminated, and that from the second case showed the gram-positive organism. Inoculation of a rabbit in the inguinal region with pure culture from the second case produced no reaction in three weeks. Both cultures have been discarded, as I do not think that they had anything to do with the lesion.

HISTOPATHOLOGY

A section was obtained from the lesion that presented normal skin on each side of the ulceration. The tissue was fixed in Zenker's fluid and paraffin sections were made and stained with hematoxylin-eosin and Mallory's connective tissue stain.

Fig. 3.—Results obtained by the intravenous medication with a 1 per cent. solution of tartar emetic. All lesions are healed except a very small line in the lesion on the thigh, the elephantiasis remaining.

Epidermis.—The most marked change in the epidermis was found at the margin of the granulomatous process; here the epidermis was greatly thickened, distorted, and folded on itself, showing attempts at regeneration and epidermization of the ulcer base, which, however, were aborted by the onward progress of the infection. This is well shown in Figure 6. The epidermal papillae at the edge of the lesion shows

marked proliferation and penetration downward into the papillary and reticular stratum. This penetration downward occurs for some distance from the edge of the lesion toward the normal skin, as shown in Figures 7 and 8. A few fissures are seen near the edge of the lesion that are partly filled with exudate which is undergoing organization, with a downward growth of epithelium, in an attempt to cover over the gap caused by fissuring. The epidermal papillae shows marked proliferation, as evidenced by the irregular edges and their penetration downward, with some of the basal cells entirely separated from the papillae. There are also offshoots from the papillae, which are about

Fig. 4 (Case 2, J. B., Negro).—Typical lesion completely encircling the base of penis, with extension onto the scrotum and into the pubic region. A typical papule is seen at the bottom of the scrotum, which has not ulcerated. This case also shows marked elephantiasis of the penis, which measured 8 inches (20 cm.) in length and 7½ inches (19 cm.) in diameter.

three cells in thickness, which penetrate the subdermal layer for some distance, ending by club formation of the epithelial cells.

As the base of the ulcer is approached beyond the edge of the lesion, we find almost complete loss of the epidermis. Here and there, we find islands of epithelium, while in other areas we only have the papillae remaining, with granulation tissue springing up between and separating the papillae. Some of these papillary buds show prolifer-

ation up to the stratum ludicium, and from these papillary buds the older parts of the lesion are epithelized; while in other areas the papillary buds are almost covered with the interpapillary buds of granulation tissue. Some of these buds of granulation tissue are quite fibrotic, as shown by the dense adult fibrous tissue (these dense nodules of fibrous tissue present a shotty feel when the hand is passed over the surface, and also produce the irregular ulcer base). There is some infiltration of the epidermis with polymorphonuclears, which we find in the intercellular spaces, the infiltration not being marked except at the ulcer margin. The cells of the epidermis retain their shape and are not much distorted except at the edge of the lesion. The prickle cells show the characteristic intercellular spines. There is, however, an increase

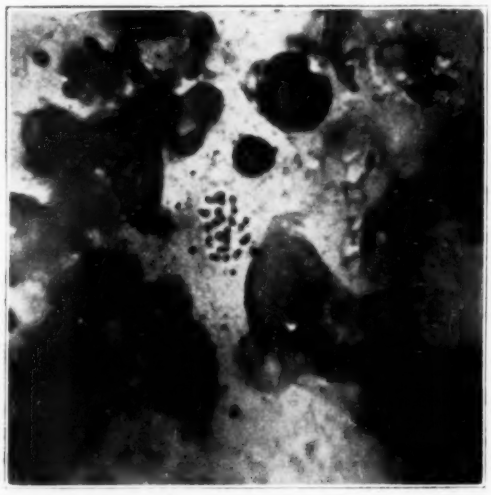

Fig. 5.—Smear from Case 1. Photomicrograph showing the encapsulated organisms occurring in a vacuole in the cytoplasm of an endothelial leukocyte. The different forms of the organisms can be distinguished: coccoid, bipolar, and short rods. All have a distinct capsule. (Oil immersion.)

in the size of the basal cells of the epidermis with proliferation. Mitotic figures were not present. There is complete loss of the pigment that is normally found in the basal cells, which is so conspicuous in the black race. Sections taken from the base of the penis or the inguinal regions show fissures that are nothing more than hair follicles that have lost most of their characteristics.

The papillary and reticular stratum of the corium which is composed of fibrous tissue, elastic fibers, and connective tissue cells which run parallel to the epidermis has been replaced by granulation tissue containing numerous blood vessels, with diffuse cellular infiltration (com-

pare Figures 7 and 8). The connective tissue cells and collagen fibrils in the papillary and reticular stratum run more or less perpendicular to the epidermis (Fig. 8).

The granulation tissue is very cellular and shows some sclerotic changes as the margin of the ulceration is approached, which is more evident beneath the ulcer base. Here, the connective tissue is very dense and the cells are more widely separated by the intervening collagen fibrils. The granulation tissue is very vascular, containing numerous large and small capillaries intermingled with angioblastic loops. They are not congested, only showing a few red and white cells in their lumina, while others are entirely void of cells. All of the larger vessels show perivascular cellular infiltration, this same type of cellular infil-

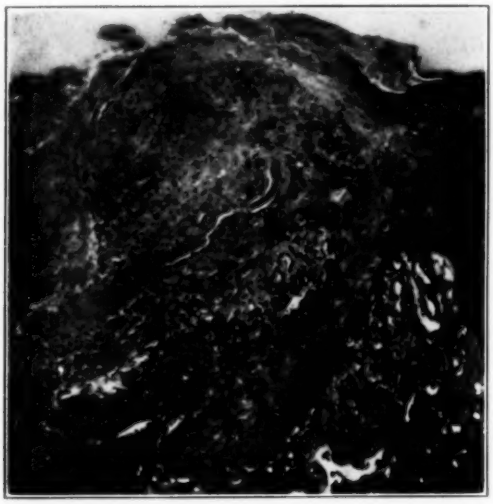

Fig. 6.—Photomicrograph of ulcer edge, showing attempts at epithelization of the ulcer base, which has been aborted by the onward progress of the disease, causing overproduction of epithelium at this point. This gives the edge of the ulcer its everted, elevated, indurated appearance.

tration being found surrounding a few remaining hair follicles and sweat glands.

There is considerable brown pigment found throughout the corium. The pigment occurs in clumps just beneath the papillae of the epidermis and in other areas it is more deeply situated. The clumps of pigment seem to bear a relationship to some type of cell, either the connective tissue or the endothelial cell, as evidenced by a nucleus which stains a dark purple, situated at the periphery or in the center of some of the pigment clumps. From the staining properties and the phagocytic character of the endothelial leukocyte, it is most probable that the

pigment has been taken up by this cell. The pigment is that which has been disassociated from the basal cells of the epidermis, or it is hemosidirin, resulting from repeated small hemorrhages that have taken place in the tissue, or a product from the connective tissue cell. If from one of these sources, it would act as a foreign body, and as the endothelial leukocyte is the chief phagocytic cell in the lesion, it points all the more to the pigment's being contained in the endothelial cell.

The most characteristic feature found in the corium is the dense round-cell infiltration, which is diffuse except some distance from the edge of the lesion. Here we find less granulation tissue, and the infiltrating cells appear more circumscribed, somewhat resembling tubercle formation, no giant cells, however, appearing here or in any other part of the lesion. This diffuse cellular infiltration is composed

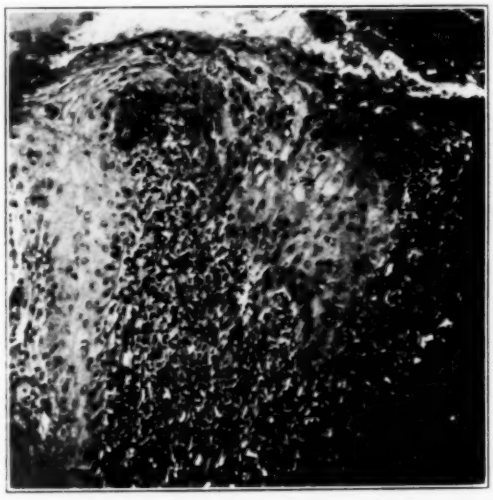

Fig. 7.—Photomicrograph showing marked proliferation of the papillae of the epidermis and their elongation downward into the papillary layer; also the granulomatous subdermal tissue with diffuse round cell infiltration. This is near the ulcer margin.

of polymorphonuclear, lymphoid, endothelial leukocytes, and a few plasma cells. Near the margin of the lesion and extending on both sides, the predominating cell is the polymorphonuclear, which is situated for the most part in the papillary layer of the corium, while in the reticular stratum we find very few polymorphonuclears, but large numbers of lymphoid cells and endothelial leukocytes, the endothelial leukocyte predominating. In some areas, we find epithelial cells that have been completely separated from the branching papillae of the epidermis. In one area I found pearl formation of these separated epithelial cells. If one is not careful, when this pearl formation is

found, the lesion may be interpreted as early carcinoma spinocellulare. It is possible that this condition occurs more frequently when the lesions occur on the glans penis or in the single ulcerated papule, as in these lesions the granulations are more cauliflowerlike, clinically resembling carcinoma.

The tela subcutanea, which extends from the inner boundary of the corium to the fascia subcutanea, is normally composed of fibro-elastic tissue (the reticulum), and large amounts of fat, with hair follicles and sweat glands lodged in its meshes. This has been replaced by a sclerosing, round-cell, infiltrated connective tissue. The collagen fibrils are very dense and run in thick wavy bands in a purposeless fashion, the fibrous tissue resembling that seen in keloids, and characteristic of

Fig. 8.—Photomicrograph showing marked elongation of the papillae with considerable thickening of the epidermis. The papillae penetrate the papillary layer for some distance. Here the granulomatous condition of the subdermal tissue is plainly seen, with numerous small blood vessels and angioblastic loops; however, they are not congested. There is marked round cell infiltration in this area. This condition is found some distance from the ulcer margin.

that type of lesion. Mallory's connective tissue stain brought out the beautiful interlacing dense wavy bundles of the fibrous tissue and all of its minute ramifications, showing that the greater part of the section was composed of connective tissue. Some of the bundles are very compact, staining a homogeneous pink with eosin. The connective tissue cells are widely separated by the intervening bands of collagen fibers. These bundles run in different directions, shown in Figure 11, and are separated in some areas by round-cell infiltration (Fig. 9).

There are large and small nests of cells scattered throughout the tela subcutanea, which are surrounded by these dense bundles of connective tissue, shown in Figure 10. The fibrous tissue around the blood vessels, hair follicles and sweat glands is more cellular than in other areas. There are numerous blood vessels present, and the majority of them show marked congestion, containing large numbers of red cells and few white cells. There is marked cellular infiltration surrounding the blood vessels, hair follicles and sweat glands.

The cell nests in this area resemble tubercle formation, as there are large accumulations of endothelial leukocytes, with a few lymphoid and fibrous tissue cells and angioblastic loops, showing that there is an active process going on in these areas, which is due to the presence of

Fig. 9.—Photomicrograph showing a marked productive fibrosis that has taken place in the tela subcutanea, with infiltration of round cells between the fibrous bundles. The blood vessels are more congested in this area. (This and the following pictures show the changes that have taken place below the base of the ulcer).

the encapsulated organisms. The predominating cell in the tela subcutanea is the endothelial leukocyte, with a few lymphoid cells and eosinophils.

In order to demonstrate the presence of the organisms in the tissue, and to ascertain their location, whether they were superficial or occurred throughout the section, I stained the tissue by the methods of Wolbach and Gram, both methods demonstrating the organisms. The organisms were found throughout the entire section of tissue from just beneath the papilla of the epidermis and interpapillary tissue to the deepest

part of the section. They appeared in colonies and were most numerous where there was a large accumulation of cells. The largest numbers being found in the corium and tela subcutanea; they were scanty beneath the epidermis. The organisms also occurred between the bundles of connective tissue where the cellular infiltration was very scarce, and in areas where they were entirely absent. The organisms seem to bear the same relation to the endothelial leukocyte in the tissue as in the smears.

In studying the tissue stained by the foregoing methods, I find that the chief infiltrating cell is the endothelial leukocyte.

The pathologic picture of the disease is that of a sclerosing granuloma.

SYMPTOMS AND CLINICAL COURSE

The age of onset is between 20 and 40 years.

Incubation.—The length of the incubation period is not known (Hoffman[14]). In one of my cases, the incubation period was a month. The disease usually manifests itself after sexual intercourse, and commences as an elevated papule, either primary or secondary to some type of venereal infection, which in the male is usually on or near the penis, and in the female, on the fourchette or labia minora. This papule may or may not cause any inconvenience. There may be a slight burning or itching sensation. The skin covering the papule is soon thinned out and is easily abraded, and a small ulceration may begin, which has a slight irritating discharge. The papule begins to increase in size and spread, the rate varying greatly in different cases. The disease spreads superficially, involving skin and mucous surfaces or both, and its advance is accompanied by new granulations at the spreading edge. This gives the edge a rolled-out elevated appearance, which is hard and indurated to the touch. This is due to the folding up of the epithelium, as described under the pathology. The granulations at the edge of the lesion are very coarse and, if curetted away, small white particles, oatseed in size, are obtained, being composed of sclerosed fibrous tissue. The whole mass appears as a coarse granular raised growth with serpiginous outlines, as a rule, without deep ulcerations except in those parts that have been excoriated and cracked from the discharges and in which secondary infection has occurred.

As the lesion spreads into the hairy parts, especially the pubic and inguinal regions, the hairs drop out. However, a few remain in the ulcerated area. The older areas are smoother and have a moist, shiny, glistening appearance, which is due to partial epidermization of the lesion, coming from the papillary buds of epithelium. These areas are

14. Hoffman, W. H.: Das Venerische Granulom, München med. Wchnschr. **67**:159 (Feb.) 1920; abstr. Surg. Gynec. & Obst. **31**:150, 1920.

more depressed and are often converted into dense white fibrous tissue. The hand passed over this surface finds it irregular, and shotlike nodules are felt just beneath the surface, probably due to the interpapillary buds of granulation tissue that has undergone sclerosis and contraction. This contraction of the underlying fibrous tissue often causes puckering of the surrounding skin.

In the great majority of cases in the male, the lesion is on, or near, the penis, and when situated on the glans penis is more exuberant and cauliflowerlike. This condition is often interpreted as carcinoma, and the penis, and when situated on the plans penis is more exuberant and cause of amputation in Case 1.) When the lesion is situated on the glans, the part is much distorted. The granulations are very coarse,

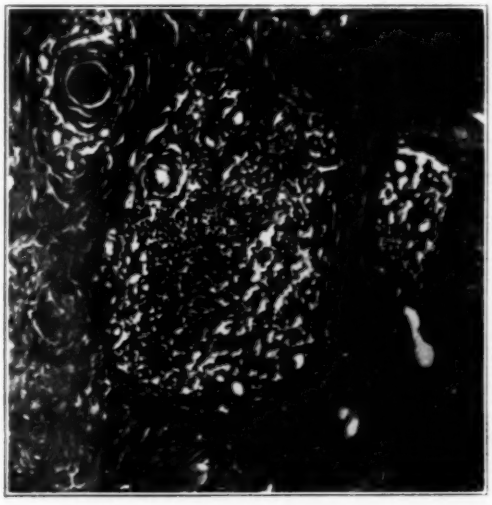

Fig. 10.—Photomicrograph showing typical cell nest of endothelial cells surrounded by dense bands of connective tissue. Perivascular and periglandular cellular infiltration can also be seen. In these cell nests and around the blood vessels, hair follicles and sweat glands, the fibrous tissue is rather cellular.

usually concealing the meatus and sometimes extending into the urethra, but only for a very short distance. When the lesion becomes annular on the penis, the formation of fibrous tissue beneath the urethra, with its resulting contracture, may cause typical cordee or a troublesome stricture.

The lesion not only spreads by direct cutaneous eccentric peripheral extension, but also by secondary papules that appear near the creeping edge, which break down and ulcerate, coalescing with the primary lesion; also by autoinoculation, which is responsible for the appearance, in the groin or base of the penis, of discrete nodules, which are probably set up by the penile ulceration or its discharges. The groin is the

favorite site of the ulceration, which extends along the soft, moist folds, or into the most hairy parts; and it is usually limited to these areas. From the folds of the groin, it may spread between the scrotum and thigh on one or both sides. In long standing cases, it creeps slowly onto the perineum and backward around the anus into which it sometimes extends for a short distance, causing an anal discharge of serosanguineous fluid. This extension backward is due to the excoriating action of the discharge which contains the organisms, which runs between the fold of the thigh and scrotum onto the perineum.

In the female, the earliest lesion is probably on the labia minora or fourchette. The lesion spreads along the cutaneous surfaces and the labia majora are soon involved. The perineum, even when the labia

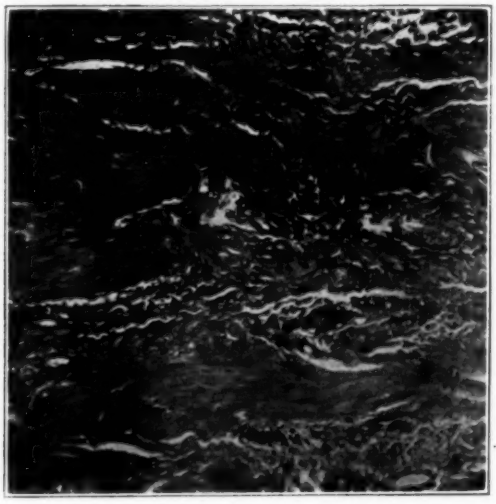

Fig. 11.—Photomicrograph showing the formation of dense wavy bands of connective tissue occurring in the tela subcutanea, with infiltration of round cells between the bundles. This, as well as other areas in the tela subcutanea, simulates very closely the fibrous formation that is found in keloids.

majora are not involved, is affected early, and the lesion then passes backward, surrounds the anus and extends into the rectum, in long standing cases. Sometimes, it extends forward between the thighs, and then, by direct continuity, may invade one or both groins. The lesion may extend into the vagina, it usually does in old cases, but this may take place very early in some cases. The involvement of the vagina may extend up to the cervix (but never invades it.—Daniels [15]).

15. Daniels, C. W.: Granuloma Inguinale in Allbutt and Rolleston System of Medicine **2**:708, Part 2, 1907.

The result of the disease is more serious in females than in males. When the mucous surfaces of both vagina and rectum are invaded, although there is no manifest sloughing, the lesions in the vagina and rectum seem to become continuous with each other through the thin fascial rectovaginal septum. In old cases, this progression of the disease along the rectovaginal septum finally results in rectovaginal fistula, which may be multiple. Ulceration either on the cutaneous or mucous surfaces is a secondary process, since the tissue, though vascular, is of low vitality and the epithelium is softened from the discharges and sodden dressings that these unfortunates wear.

In countries in which the disease is common, there are distinct variations, depending on the rapidity of extension, the varying tendency to form scar tissue, as well as the part involved. The disease is more destructive on mucous than on cutaneous surfaces, and spreads more rapidly when there is a certain amount of moisture present. When situated on the external parts of the thighs, the abdomen, or the neck, or in other places that have a relatively dry surface, the lesions remain localized, with no tendency to extension.

The lymphatic glands are not enlarged nor does suppuration take place ("a diagnostic point"). Daniels [15] writes: "There must, however, be some obstruction of the lymphatics, as a chronic edema, spurious elephantiasis of the vulva, penis, or scrotum is common without any evidence of filarial elephantiasis." The scrotum, penis and vulva under the foregoing conditions become very large and pendulous at times and produce considerable discomfort to the patient in walking.

Duration of the Disease.—The disease shows marked chronicity, extending over a period of from five to fifteen years without marked improvement in the condition. It is not manifested by any marked constitutional symptoms; although some of the cases show different grades of anemia, the general health is little affected.

Diagnosis.—The disease must be differentiated from tuberculosis, syphilis, cancer and chancroid. As a rule, this is not difficult; but at times it is very trying, and a diagnosis is settled only by resorting to various laboratory tests. The typical history, the long duration, finding the Donovan bodies in smears from the lesion and the typical pathology displayed by the disease clinch our diagnosis. The development is more slow than that due to tertiary syphilis and more rapid than that of tuberculosis. The resemblance to tertiary syphilis is often very close, and, as very frequently happens, the disease is complicated by syphilis. A routine blood Wassermann test should be made on all cases.

Sometimes, the lesion very closely resembles carcinoma, especially when situated on the glans penis, as here the granulations seem to be more exuberant.

It is easily differentiated from chancroid by the sclerosing, everted rolled-out edges, in contrast to the undermined edge of chancroid, with negative inguinal glands.

Any patient presenting a chronic, sclerosing, serpiginous ulceration of a granulomatous type, on or near the external genitals, should be thoroughly examined for evidence of granuloma inguinale.

TREATMENT

Since the first reported case, granuloma inguinale has been treated locally by various methods, such as salves, lotions, curetment, cautery, surgical excision, roentgen ray, and internally by the iodids, mercury, arsphenamin and antimony.

Salves and lotions are only mentioned to condemn them (with the possible exception of tartar emetic incorporated in an ointment to be used externally), as their action only increases the discomfort of the patient. Curetting the lesion very thoroughly until all the diseased tissue has been removed has brought about a cure in some cases. From the location of the organisms in the tissue, it seems highly improbable that curetting away all of the granulation tissue will secure a cure of the disease. After all granulation tissue has been removed, one comes to a hard shiny surface, which is the beginning of the sclerosing part of the lesion beneath which there are large numbers of organisms that cannot be reached with the curet. One can readily see why a recurrence takes place through failure to get rid of all the organisms. The same thing holds true for the use of the cautery, but more successful results have followed the use of the actual cautery. It may be used in some cases, but the results, as a rule, are very disappointing.

Surgical removal has been used with some degree of success, as quite a number of cases have been reported cured by this procedure. In India, the results have been very encouraging in these cases of surgical removal. If surgical excision is decided on, it should be carried out thoroughly and the lesion should be dealt with as if it were malignant. All the diseased tissue should be removed along the lines of débridement, and every effort should be made to prevent contamination of the wound. The cautery knife should be very efficacious in this procedure. In selecting cases for surgical excision, the lesions should be located in accessible parts where wide excision can be made; otherwise, the results will not be encouraging. I believe the surgical treatment of granuloma inguinale should be limited to those cases that occur in old people, especially those suffering from kidney lesions, as in these cases tartar emetic may aggravate the kidney lesion and produce serious results.

The use of the roentgen ray locally has proved satisfactory in some hands. De Souza-Araujo, quoted by Low and Newham,[16] reported a cure by roentgen-ray treatment in 1915; in Brazil, and drew attention to the pioneer work of Macleod and Sequiera in this connection. In one of my first cases, the patient received nine roentgen-ray treatments without any noticeable improvement of the condition.

The internal administrations of the iodids, mercury and its salts, and arsphenamin, seems to have no beneficial effects on the course of the disease, except when it is complicated by syphilis. If syphilis is present as shown by a positive Wassermann reaction, the patient should receive active antisyphilitic treatment, and, in the rest period of the treatment, should receive tartar emetic intravenously; that is, tartar emetic should be alternated with the treatment for syphilis. Lynch [9] of Charleson, S. C., suggested this method, which is a most excellent one.

Antimony was first used in tropical medicine by Mensil and Nicalle [17] for trypanosomiasis, in 1906. Pliumer and Thompson [17] followed this by employing the potassium and sodium tartrate of antimony in rats infected with such parasites. Subcutaneous injections cleared the parasites from the blood quickly. Sir Patrick Manson [17] tried similar treatments on human patients in 1907, but the local reaction was so severe that he had to abandon the treatment. About this time, Broden and Rodhain,[17] and independently of them, Lebouf,[17] tried intravenous injections of tartar emetic in natives of West Africa suffering with sleeping sickness, without bad effects, and with rapid improvement. Still later, Kerandel [17] became infected and treated himself with completely satisfactory results. Stimulated by these results, different authors have employed it intravenously for this condition, and for American leishmaniasis, Mediterranean and Indian kala-azar, and oriental sore.

To Argão and Vianna [17] of Brazil, in 1913, we are greatly indebted for its use intravenously in the treatment of granuloma inguinale. And since then, its use has become universal in the treatment of this disease.

In the use of tartar emetic intravenously, great care should be exercised to prevent the drug being infiltrated in the subcutaneous tissue around the vein, as such infiltration is exceedingly painful and in large amounts may cause troublesome sloughing of the tissue similar to that which results from arsphenamin when it infiltrates around the vein. In old people suffering from debility and those having kidney lesions, great care and judgment should be used, as fatalities

16. Low, G. C., and Newham, D.: Ulcerating Granuloma, Brit. M. J. **2**:387 (Sept. 16) 1916.

17. Quoted by Law and Newham, Footnote 16.

have resulted from its use in such cases. In this type of patient, surgical removal combined with very weak solutions of tartar emetic should be used. If tartar emetic is used, the urine should be watched very closely.

Tartar emetic seems to be used universally in a 1 per cent. solution, and the dosage varies in different hands, some using as much as 20 c.c. of the solution at a time.

In preparing the solution, dissolving the tartar emetic in distilled water has been advised, then passing it through a Berkefeld filter until, on culture, it is negative. Five-tenths cubic centimeter of hydrochloric acid is added to prevent precipitation. We have not followed this method in the preparation of our solution, but use a much simpler method, which has given us gratifying results in our cases. The method that we use is as follows: To 100 c.c. of distilled water, 1 gm. of tartar emetic is added, the drug having first been finely powdered to facilitate its going into solution; then the solution is thoroughly boiled, after which it is ready for use. A solution fixed by the foregoing method has remained perfectly clear, without the slightest precipitation, for a month. The foregoing method does not seem to affect the drug in any way as to its efficacy in curing the disease or to its producing any harmful results. The method is very simple in its application, saves time and does away with apparatus; and the curative value of the solution is not destroyed.

We have used the method of administration described by Campbell,[6] a most excellent one. We usually begin with 2 c.c. of the 1 per cent. solution diluted with 8 c.c. of sterile distilled water. The injections are given every other day, 1 c.c. more of the tartar emetic solution and 1 c.c. less of the diluent being used at each treatment, until the full 1 per cent. solution is used. We have not used more than 12 c.c. of the solution, and, at times, the patients have shown some slight reaction, such as a brackish taste, dizziness, nausea, and pains in the bones. In a personal communication, Dr. Reed, who has given the solution in a large number of cases, said that some of his patients have complained of headache, vertigo, nausea and vomiting, pains and diarrhea. We have used the foregoing plan of treatment in two cases, with complete cure of the disease and marked improvement in the general condition.

Usually, after the first two or three injections, the secretions diminish rapidly, and by the fifth injection, they have entirely ceased. Then rapid healing takes place. First, there is the drying up of the discharges; then the lesion takes on a healthy look, and epidermization rapidly takes place from the edge of the lesion, also from the islands of epithelium (papillary buds) scattered about the base. In a few weeks, from four to six, the lesion completely heals, leaving a whitish scar

which is very thick and whose underlying connective tissue is very hard and irregular. The epithelium is rather soft in texture.

After all of the lesions have entirely healed, the patient should receive weekly injections for from two to three months; then injections twice a month for at least four months. The patient should be kept under close observation for at least a year, as relapses may occur in some of the cases. As soon as the lesion is completely healed over, patients think they are well, and will not continue treatment until they have a return of the disease. This happened in Cases 1 and 2. After complete healing, the patients did not return to the clinic for two months, at which time both had recurrence. If the foregoing plan of treatment can be carried out and the patient gives full cooperation, relapses will become a negligible quantity.

The treatment of the complications, such as stricture, rectovaginal fistulas, and elephantiasis of the external genitals, should not be attempted until at least a year after all lesions have completely healed.

The first case that came under my observation was the first reported case in which Donovan bodies were demonstrated, in Louisiana. This case has been reported by Drs. Reed and Wolf.[8] I first tried surgical excision of the lesion in this case, with complete failure. The lesion was on the penis. I only mention this case to show the fallacy of surgical removal in cases in which you cannot make wide excisions.

REPORT OF CASES

CASE 1.—E. R., a negro, aged 30, visited the clinic, March 10, 1921, being referred by Dr. R. E. Stone.

There were sores on the genitals, abdomen and leg. For the last five years, the patient has suffered from a granulomatous lesion on the genitals. For the last year, he had had ulceration at the site of the suprapubic wound and a skin graft from the thigh. The ulceration entered the urethra and anus, and involved the inguinal region and the region between scrotum and thigh. There was elephantiasis of the scrotum. The Wassermann reaction was negative. Smears were positive for Donovan bodies. A section removed was pathologically typical of granuloma inguinals.

Granuloma inguinale was diagnosed.

The patient received nineteen injections of tartar emetic with complete healing of the ulcers. He remained away for two months, and returned with a recurrence. He has received twenty-five additional injections, with very slight healing.

CASE 2.—J. B., a negro, aged 30, visited the clinic, Aug. 16, 1921, complaining of a sore on the penis. One year before, a small papule had appeared at the base of the penis, gradually increasing in size and forming a serpiginous outlined granulomatous ulceration. At present, it was creeping upward into both inguinal regions and backward to the perineum. There was a secondary papule on the scrotum. The penis showed typical elephantiasis. The Wassermann reaction was negative. A smear was positive for Donovan bodies. The section removed was pathologically typical of granuloma inguinale. After eleven

injections of 1 per cent. tartar emetic, the lesions completely healed. Against advice, the patient remained away from the clinic for two months. He had a recurrence which, after nine injections of 1 per cent. tartar emetic, completely healed.

Case 3.—E. P., a negress, aged 25, who visited the clinic, Jan. 7, 1922, three months previously had had a small papule appear on the right labium minorum, gradually involving the entire external genitals. The lesion was a sclerosing, serpiginous outlined granulomatous ulceration involving the labia minora, labia majora, posterior wall of the vagina and partly encircling the anus, into which it extended. The involvement of the rectovaginal septum had almost produced rectovaginal fistulas. The Wassermann reaction was negative. Smears were positive for Donovan bodies.

The patient received four injections of 1 per cent. tartar emetic solution, with marked improvement, after which she deserted. From the involvement of the rectovaginal septum, and without proper treatment, this patient will probably develop rectovaginal fistulas.

Case 4.—N. S., a negress, aged 42, who visited the clinic, Jan. 17, 1922, being referred from the gynecologic clinic, five months before began to have severe itching of the vulva, with a vaginal discharge. There was a pronounced granulomatous lesion, involving the labia majora, which were hard and everted, the labia minora, the fourchette, the posterior wall of the vagina and the clitoris, which shows slight elephantiasis. The introitus of the vagina was practically closed, and the lesion was rather atypical, resembling carcinoma. There was a lesion on the inner side of the left thigh, which had very exuberant granulations. The whole lesion presented a sclerosed, serpiginous ulceration, with exuberant granulation and numerous areas, white in color, which were most probably cornified epithelium. There was a severe vaginal discharge. The Wassermann reaction was negative. Smears showed Donovan bodies. A section removed was pathologically typical of granuloma inguinale.

The patient received twenty injections, with marked improvement. Unfortunately she also deserted.[18]

CONCLUSIONS

1. The disease is a definite clinical entity. It occurs in the United States, being endemic in some states, especially in the extreme Southern States. It is endemic in Louisiana.

2. The cause is probably the organism described by Donovan, possibly a protozoa.

3. The disease presents definite clinical symptoms which extend over long periods. The symptoms vary somewhat in different persons, for the most part, showing a typical granuloma with a serosanguineous discharge.

4. The pathologic picture is that of a sclerosing granuloma.

5. Tartar emetic administered intravenously seems to be specific, although I think that when the lesions are accessible to surgical excision, this procedure combined with tartar emetic, will considerably shorten the healing time.

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18. The case histories are greatly abbreviated on account of lack of space.

6. Every patient presenting a granulomatous lesion of the external genitals with negative inguinal glands should be searched for evidence of granuloma inguinale.

7. The cases should be watched for at least a year after treatment has brought about complete healing, as this will cut down the percentage of recurrences.

1929 Napoleon Avenue.

A CASE OF DERMATOMYOSITIS

HENRY JOACHIM, M.D.
BROOKLYN

History.—P. E. C., aged 37, a fireman, married, was admitted to Long Island College Hospital, Dec. 28, 1921; discharged, Jan. 4, 1922. His chief complaints were: (1) swelling of the head, wrists and legs; (2) stiffness of muscles throughout the body; (3) the presence of lumps at the back of the head, and (4) "gastritis."

His mother died of cancer of the breast, at the age of 56. The patient had had pneumonia at the age of 4. The past history was otherwise negative.

In July, 1921, the patient noticed painless swelling of the head and neck, which necessitated an increase in the size of his collar from 15 to 15¾. He also noticed that he was rapidly gaining fat over his chest and abdomen. The swelling of the face did not cause any puffiness of the eyelids but was enough to change his facial expression by obliterating the folds of the forehead. There was distinct pitting over the forehead and neck, but no redness, tenderness or itching. This continued for seven weeks. In the latter part of July, the patient noticed a dull ache and heavy sensation of both upper extremities from the elbows to the shoulders. He described it as a "sensation a person would have who had been carrying some heavy weight at his side and then tried to raise and stretch his arms up over his head." It necessitated a distinct effort to overcome this sensation of soreness which was intensified when the patient raised his arms over his head as in fastening his collar at the back. This persisted for ten weeks. Accompanying this soreness, the patient noticed swelling of the forearm, wrists and hands. There was definite pitting. He was unable to clench his fist. One week later, both legs became swollen, more particularly the left. The feet were not involved, but the swelling extended up to the inner side of the left groin. It was less in the morning, increasing toward evening when the patient was up and about. About this time, there was a tightness and stiffness of the muscles all over the body.

About the beginning of October, the patient began to note definite discrete lumps behind his ears and the back of the head. The first lump appeared about the middle of September, hard, red, itchy and painless. It was about the size of an egg and disappeared entirely the next morning. The next night a similar lump, somewhat smaller in size, appeared behind the left ear, but was gone the next morning. These recurred for a period of about three weeks. About the same time, there was extreme swelling of the skin of the penis, which varied in intensity, usually being worse at night or after prolonged standing. About the middle of September, the lips became swollen. This condition was more marked after his morning meal, and lasted about two weeks. He experienced some difficulty in opening the jaws widely as the face had a sensation of tightening. At about this time, there was an eruption of "small pimples" at the edge and tip of the tongue and at the inner surface of the cheeks, and his mouth felt sore. Borax was applied, and the mouth and tongue improved, in ten days.

At about this time, the patient complained of palpitation, more marked at night. He also noticed that he tired very easily on exertion. In October, he began to have epigastric distress after eating. He was placed on a vegetable diet, and in about three months lost 25 pounds (11.3 kg.) in weight. He was then referred to the hospital for study, in December.

Fig. 1.—Atrophy, swelling of fibers and vacuolization.

Fig. 2.—Atrophy, swelling of fibers and vacuolization.

Physical Examination.—The patient was about 5 feet and 11 inches (1.8 meters) tall, and weighed 160 pounds (72.7 kg.). His hair was thin and dry, his cheeks were sunken, and the skin of the face was dry and adherent. The skin over the sternum was brown, scaly, dry and adherent; the skin about the arms, forearms and hands smooth, dry, shiny, tense and unable to be raised from the underlying structures. The skin of the left side of the abdomen presented the same condition. The left thigh and leg, in addition to the skin changes described, were markedly edematous. The patient experienced some difficulty in making a fist on account of tightness of the skin of the hands. The ears were slightly cyanotic. Examination of the heart revealed the apex beat 10 cm. from the midsternal line in the fifth interspace; there was a systolic blow at the apex, not transmitted. The pulse rate was 124. Fine capillaries were noted at the costal margin. The lungs were negative; the liver and spleen not palpable. The reflex of the right upper abdominal quadrant was absent; the knee jerks were exaggerated. The temperature ranged from 98.2 to 100.4 F. (rectal).

Diagnosis.—From the history and physical examination, the following possibilities were considered: (1) scleroderma; (2) myxedema; (3) deficiency edema from beriberi or scurvy; (4) trichinosis; (5) dermatomyositis, and (6) trophoneurosis (angioneurosis).

Laboratory Procedures.—The basal metabolism was reported as plus 25. With this finding and the tachycardia, we felt we could exclude myxedema. A sugar tolerance test was not made.

Complete blood count revealed: hemoglobin, 70 per cent.; red blood cells, 4,860,000; white blood cells, 10,800; polymorphonuclears, 72 per cent.; lymphocytes, 28 per cent. In the absence of an eosinophilia, it seemed that trichinosis and anaphylaxis could be excluded.

The feces were negative for parasites and ova, and there was no blood present. The Wassermann reaction was negative. Thirty-eight food protein skin tests were made with the ordinary food proteins, but all were negative.

Test of the blood chemistry revealed: urea nitrogen, 27.2; urea, 58.4, uric acid, 3.33, and creatinin 1.58 mg. per hundred cubic centimeters of blood; blood sugar, 100. The blood gave evidence of some nitrogenous retention. Urinalysis revealed: urine, neutral, negative; specific gravity, 1.028. A renal meal gave a specific gravity varying from 1.022 to 1.032. The blood pressure was 125 systolic, 65 diastolic.

Fluid intake and fluid output were about equal.

The patient was referred to Dr. Potter, December 31, who thought that the diagnosis of dermatomyositis was the most probable one. We advised excision of a piece of muscle for histologic and bacteriologic study. Dr. Oliver cultured a specimen of excised muscle and reported no growth.

Histologic Findings (Drs. Murray and Coulter).—The muscle fibers show profound degenerative changes of two kinds. In the first, the fibers are greatly swollen, to four or five times the normal diameter. In some areas the fibrils are separated from one another but retain their striation; occasional large vacuoles are seen within the muscle sheath. In other areas the striation is wanting and the fibers appear uniformly hyaline and deep-staining with eosin. These changes are also seen combined in single fibers. The sarcolemma nuclei are normal, or are small and pyknotic. There is no wandering cell infiltration in muscle bundles so affected.

In the second type of degeneration, which represents apparently a later stage of the first, and for the most part involves uniformly separate muscle bundles,

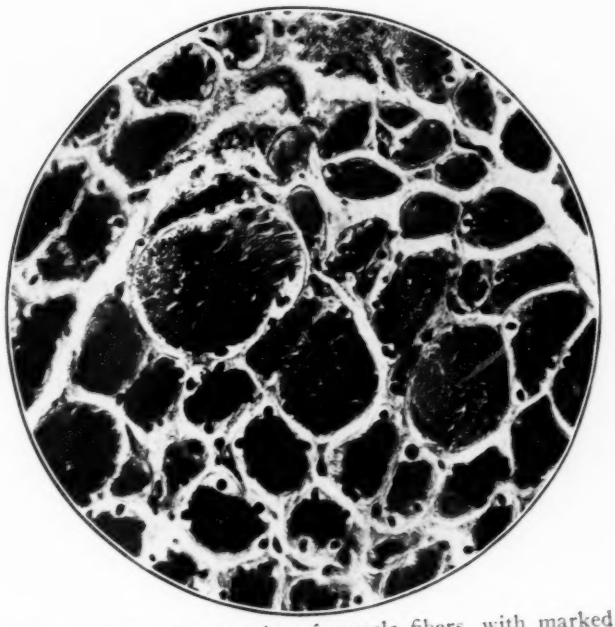

Fig. 3.—Hypertrophy and atrophy of muscle fibers, with marked variations in size.

Fig. 4.—Hydropic degeneration of muscle fibers.

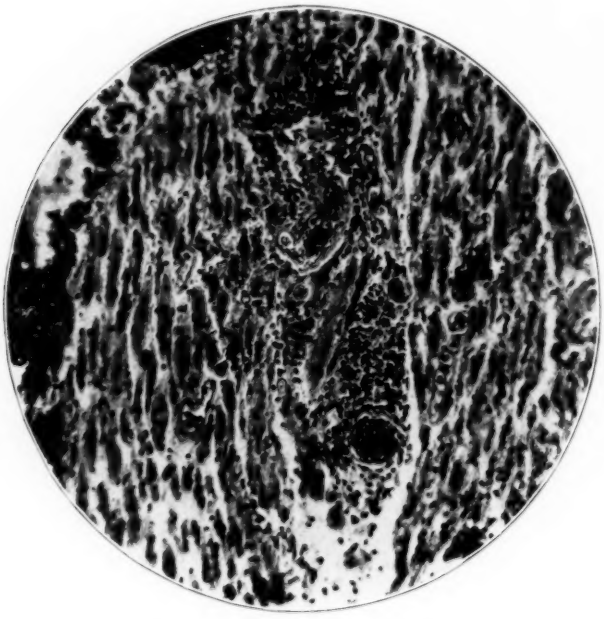

Fig. 5.—Diffuse round-cell infiltration and congested vessels.

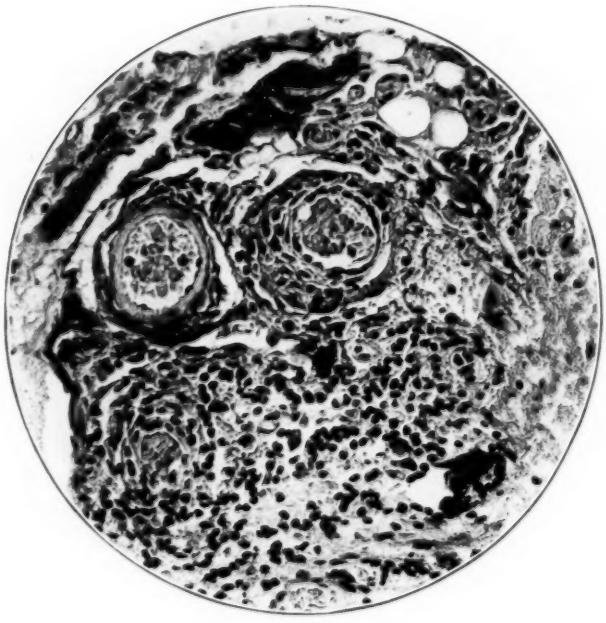

Fig. 6.—Small round-cell infiltration, especially about the veins.

the fibers are much reduced in size or have disappeared; they are hyaline and contain occasional vacuoles. The spaces between the fibers are filled with edema fluid. The sarcolemma nuclei are large and increased in number. Some muscle fibers contain from one to six or more large vesicular nuclei and appear to be in process of regeneration.

The areolar connective tissue between the muscle bundles is edematous and contains many wandering cells; some scattered, others grouped about and within the walls of the smaller blood vessels or in isolated clumps. Approximately 50 per cent. of the cells are polymorphonuclears; the rest are plasma cells and small mononuclears. Some of the wandering cell nuclei stain faintly, and the cell appears necrotic. Inflammatory cells are seen also in groups at the periphery and scattered diffusely within the bundles of atrophic muscle fibers. Numerous small hemorrhages are seen within the intermuscular connective tissue. There is no increase in fibrous connective tissue and developing fibroblasts are not seen.

The subcutaneous areolar and fatty tissue is edematous and contains occasional small hemorrhages. There is a perivascular infiltration of plasma cells and lymphocytes about the smaller blood vessels.

871 Park Place.

THE PATHOGENESIS OF MERCURIAL STOMATITIS

WITH A REVIEW OF THE LITERATURE ON MERCURY POISONING

DANIEL H. BESSESEN, M.D.

MINNEAPOLIS

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INTRODUCTION

In undertaking a study of the pathology of mercurial stomatitis, I was surprised to find that most of the theories advanced to explain those changes embraced secondary alterations or were far too narrow in their scope. In order to endeavor to explain the mouth lesions, it is necessary to comprehend the changes produced in other parts of the anatomy and then to attempt to piece all the findings together, in an effort to show that the lesions in the mouth depend for their origin as much on the general changes as on the local findings. It would be well, then, to place before the reader the most important observations made by investigators of mercurial poisoning in the past.

THEORIES

The theories which relate to the pathogenesis of mercurial poisoning may be set down as follows:

1. There is direct irritation with resulting inflammation. In conjunction with this would appear the hypothesis (or fact) that saliva and bile secrete mercury; and because of that fact an endeavor is made to explain why the crests of the intestinal folds are most affected. This view is now held to be obsolete by the later writers on mercury poisoning, and is considered only an auxiliary factor in those cases in which the mercury is administered by mouth.[1]

2. The excretion of the mercury through the mucous membrane causes a poisoning and necrosis of the tissues (Schmeideberg, Fränkel, Falkenberg, Marchand, Kraus, Kokert, Paulson and Priebatsch).[2]

3. There is a disturbed secretion—the mercury is precipitated before it is excreted and therefore it cannot be eliminated (Meyer and Steinfeld).[3]

4. Cramps in the muscular tunic force the dilated veins against the intestinal content, rupturing them, producing submucous hemorrhages, with resulting slough; hence, the intestinal ulcerations. This theory is supported by Grawitz.[4]

5. Fall of blood pressure acts as the predominant factor, or at least as a supporting causative factor (Kunkel, Grawitz, Eckmann).[5]

6. As a result of coagulation in the capillaries, a nutritional disturbance of local nature presents (Kaufmann, Kunkel).[6]

7. A specific bacterium, present normally in the mouth, is stimulated or allowed to multiply without check by the administration of the mercury (Rona, Loblowitz).[7]

8. Mercuric sulphid is formed by the hydrogen sulphid thrown off by the bacteria in the mouth and colon, and by the mercury in the blood which deposits in the capillary endothelial cells and causes disturbance of nutrition and resulting necrosis and slough (Almkvist).[8]

9. Mercury is more active in the absence of salts and albumins; hence, the localization of the lesions (Sabattani).[9]

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1. Sabattani, L.: Physikalisch-Chemisch Betrachtungen über die Pharmakologischen und toxische Wirkung von Quecksilber, Biochem. Ztschr. **11**:294-310, 1906. Almkvist, Johann: Ueber die Pathogenese der merkuriellen Colitis und Stomatitis, Dermat. Ztschr. **13**:827-864, 1906.

2. Sabattani and Almkvist: Footnote 1. Priebatsch, George: Ueber die Grundwirkung des Quecksilbers, Arch. v. Anat. u. Path. **201**:192-207, 1908.

3. Sabattani and Almkvist: Footnote 1. Weiler, F.: Die anatomischen Veränderungen bei der Sublimatvergiftung des Kaninchen in ihrer Abhängigkeit von Gefässnervensystems, Virchow's Arch. f. path. Anat. **212**:200-224, 1913.

4. Almkvist: Footnote 1, second reference. Weiler: Footnote 3, second reference: Kunkel: Ueber die akute Quecksilbervergiftung, Sitzungsb. d. phys.-med. Gesellsch. zur Würzb. 1889.

5. Almkvist: Footnote 1, second reference. Siebert, K.: Ueber Stomatitis mercurialis und ihre Verhütung durch Isoform-Zahnpasten, Deutsch. med. Wchnschr. **33**:256-260, 1907.

6. Almkvist: Footnote 1, second reference.

7. Sabattani: Footnote 1, first reference.

Clinical Appearance in Mercurial Poisoning

CHARACTERISTIC SYMPTOMS

There are certain characteristic symptoms of mercury poisoning which are not dependent entirely on the amount taken, but vary according to the patient, influenced, of course, somewhat by the quantity of drug administered.

Karvonen classified these symptoms as follows.[8]

Severe Cases: There is a fall of blood pressure and heart activity; a small, often frequent, pulse; cool, sweaty, cyanotic skin; dyspnea; often psychic alterations—usually unrest and sleeplessness; often, also, later, deep apathy and comatose condition, paresthesias, paralysis and subnormal temperature.

Less Severe Cases: Gingival paleness, fatigue, lassitude, oliguria with cylindruria, and albuminuria.

Mild Cases: Simultaneously with or earlier than polyuria, the intestinal lesions attract attention. There are anorexia and cutaneous eruptions. There may be sudden death from cardiac failure. When the foregoing symptoms come on suddenly, life is in danger. Usually death occurs after progressive prostration.

Subacute Poisoning.—There occur anorexia, emaciation, albuminuria, cylindruria, diarrhea and cachexia. In men, stomatitis is the commonest symptom and intestinal destruction; more rarely, there are kidney lesions.

Chronic Poisoning.—In these cases, we find cachexia, anorexia, parenchymatous degeneration of organs; fatty heart, liver and kidney; changes in bone marrow; even interstitial changes in organs. In men, stomatitis, dysentery, kidney lesions, cachexia and nerve lesions—as tremor, irritability, rarely paralysis or psychic destruction—are the rule. Variations occur which make for difficulty in diagnosis.

In the final stages there occur loss of heart muscle force, inanition, uremia and primary alterations of the central nervous system.

BLOOD CHANGES

J. Von Mering[9] (1880) finds that there soon occur a high grade anemia, emaciation and loss of appetite with muscle weakness.

Bockhart[10] (1885) thought the whole trouble was that the insufficiently oxidized mercury in the tissues increased the reduction processes

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8. Karvonen, J.: Ueber den Einfluss des Quecksilbervergiftung auf die Nieren, Dermat. Ztschr. **5**: 1898.

9. Von Mering: Ueber die Wirkung des Quecksilbers auf den tierischen Organismus, Arch. f. exper. Path. u. Pharmakol. **13**:86-117, 1880.

10. Bockhart, W.: Ueber die Aetiologie und Prophylaxe der merkuriellen Stomatitis und Proktitis, Monatschr. f. Prakt. Dermat. **34**:113-121, 1902.

already present. This injures and weakens the structures and gives favorable conditions to the micro-organisms.

Edward Kaufmann [11] (1888) reports that the red blood cells diminish and the white blood cells increase in mercury poisoning. The red cells diminish with each dose as if there is a cumulative action. If the dose is increased, the paucity is increased. Shortly after the injection, the red cells are pale and granulated. Peptonates and albuminates of mercury are soluble in serum and exercise a destructive action on hemoglobin. Kaufmann refers to Dolen and Butte, who assert that the oxygen absorbing power of the blood is not altered by mercury; that there is a fall of the red cell count from 4,500,000 to 2,700,000, and varying; also, that the urinary substances in the blood increase five or six times the normal amount. Kaufmann and Heilborn find the gallbladder tightly filled, with an increase in bile production.

Kunkel [12] (1889) says that mercury poisoning is a blood poisoning; it leads to changes, dissolution and destruction of blood cells. Injections into healthy animals of the blood of mercuralized animals will cause similar changes. He used varying percentages of mercury compounds to disprove any laking action, and made blood counts whose results coincide with those which Koll made eight years later.

Koll [13] (1897) found a constant depletion of red cells following mercury injections. Typical examples of his results are as follows:

First day, 12 m., 6,084,000; second day, 1:30 p. m., 5,700,000; second day, 6:00 p. m., 5,232,000; second day, 12 m., 5,156,000; second day, 6:00 p. m., 4,800,000; third day, 5:00 p. m., 3,984,000.

First day, 11 a. m., 5,592,000; first day, 1:00 p. m., 6,180,000; first day, 5:00 p. m., 5,196,000; second day, 11:00 a. m., 4,200,000; third day, 7:00 p. m., 4,080,000; fourth day, 10:00 a. m., 3,644,000;

Karvonen [8] (1898) states that the destruction of blood cells in the vessels causes hemoglobinuria, and refers to Kobert to the effect that mercury with hemoglobin forms a stable compound (as stable as carbon monoxid hemoglobin).

Elbe [14] (1905) claims that the mercury circulates in the lymph and blood as albuminate and acts as an irritant on the nerves of the renal and iliocolic areas, causing a narrowing of the "second order," with a resulting backflow in the vessels of the colon and intestine.

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11. Kaufmann, E.: Die Sublimatintoxication, Habilitationschr., 1888.

12. Kunkel: Footnote 4, third reference.

13. Koll: Experimentelle Beiträge zur Kenntniss der akuten Quecksilbervergiftung, Würzburg., 1897.

14. Elbe: Die Nieren und Darm veränderungen bei der Sublimatvergiftung des Kaninchens in ihrer Abhängigkeit von Gefässnervensystem, Virchows Arch. f. path. Anat. **182**:445-498, 1905.

It is also of interest, because of its general bearing on the subject, that Almkvist (1903-1919), in referring to the literature, ascertained that mercury has been found in the blood and bile. Von Overbeck and Zeller found mercury in the blood and bile of animals; Buchner, in the blood of persons; Pavy, in the blood and liver; Welander, much in the blood and also in pus and ascitic fluid, but most in blood. Ludwig, Zilner and Kullman showed that blood contained mercury in mercury poisoning. Almkvist further asserts: "Chemical analysis has given no foundation to the conception that the mercury is localized in the solid tissues, but shows that in mercury poisoning, most of the mercury exists in the blood, lymph and tissue plasm. After thoroughly washing through an organ, approximately one third of the total quantity of mercury remains in the organ."

Another indication of the effect of mercury on the blood is its effect on the blood-forming organs.[8] There is hyperemia of the marrow of the long bones (Heilborn, Raimond, Königer, Prevost).[15] This fact is of importance in demonstrating the hyperactivity of the blood-forming tissue.

These reports indicate that apparently all who have investigated the subjects of blood and blood-forming tissue in mercury poisoning find some change, such as depletion of red cells, an increase in white cells, a content of mercury and hyperemia of bone marrow. No contrary observations were found in the literature.

What kind of compound the mercury makes with the blood, or at least what the action of the mercury is on the blood, is a problem for physiologic chemists. It is my impression that there is a constant and early action of mercury on the blood, probably a combination of the mercury with the hemoglobin. The hyperemia of the bone marrow is added proof of the destruction of blood with the resulting stimulation of the blood-forming organs.

THE SYMPATHETIC SYSTEM

Vascular Changes.—Heilborn[16] reports a general vascular dilatation; the vena cava is much dilated; the liver and spleen are large and solid, and the lungs hyperemic (this last is not constant).

J. Von Mering[9] (1880), in all cases, observed a fall of blood pressure. Experiments on frogs and dogs demonstrated a gradual fall of pulse rate. The two go down together. Neither administration of atropin nor section of both vagi alters this. Also a stimulation of the medulla oblongata, while it raised the pressure for a while, did not do

15. Weiler: Footnote 3, second reference.

16. Heilborn, Max: Experimentelle Beiträge zur Wirkung subcutaner Sublimat Injectionen, Arch. f. exper. Path. und Pharmakol. **8**:361, 1878.

so for long. This would indicate a lesion of the heart muscle and also of the vascular muscle or vascular nerves. The diarrhea, hyperemia of intestinal organs and injections of the cheeks are due to vascular changes.

Kaufmann [11] (1888) found a changed blood distribution in the whole abdominal cavity—a general vascular dilatation.

Kunkel [12] (1889) believed that a sulphur compound, together with intestinal contractions on dilated vessels, caused the lesions in the colon.

Marchand [17] (1891) described dilated vessels in mercury poisoning.

From Eduard Koll's work,[13] in 1897, the following passage is taken: "It is conceivable that the primary alterations of the vessel walls under the influence of the mercury circulating in them play the mediate role. That certain changes, during mercury poisoning, occur in the vessels of other organs, has been earlier ascribed. Von Mering found hyperemia of the vessels of the diaphragm and heart, accompanied by marked hyperemia of the sharply looped vessels of isolated long medullated bones; in the region of the latter, he observed cloddy, reddish brown masses, which he considered as degenerated passing red cells. There is little probability that these changes are of primary nature. Much more likely they are the consequences of either a primary or secondary circulatory disturbance."

Karvonen [8] (1898) found vascular filling an early effect in mercury poisoning—strong vascular dilatation.

Elbe [14] (1905) sees an irritant to the vasomotor nerves to the renal and ileocolic vessels, with narrowing of the arteries, which results in a necrosis of the kidney cortex and colon, presenting anemic infarcts in the former, hemorrhagic in the latter.

Weiler [15] (1913) explains a fall of blood pressure due to a weakening of the heart or the vessels or both. According to him, Kolb found a rise of blood pressure on the third day in animals; Geisbock, a rise for six days, and then a fall, in human beings. Weiler felt that the fall of blood pressure alone was not sufficient to cause the localized lesions, and he furnished from the literature the further suggestions offered by Kolb: [18] injury of capillary endothelium by hypertension; and Grawitz: the tearing of the capillaries as a result of forceful contractions of the intestinal folds on dilated vessels against the contents of the colon.

Almkvist [6] (1903-1919) observed that changes in the tongue resulted from extreme dilatation of the vessels, which may or may not occur before the "orchestra chair" ulceration, causing a swelling, with cupped

17. Marchand: Nachtrag von Wilhelm Falkenberg's Arbeit, Virchow's Arch. f. path. Anat. **123**:587-592, 1891.

18. Kolb: Ueber Blutdruckuntersuchungen bei Sublimat nephritis, München. med. Wchnschr., No. 13, p. 582-584, 1903.

crypts for the teeth. The lip and cheek changes are similar to the tongue changes. Then he asks what causes this vascular dilatation. He proceeds to explain: it is present in the stomach and small intestine as well as in the colon, and yet there is no mercuric sulphid precipitate in the two former; the dog shows no deposit of the sulphid precipitate, yet it demonstrates vascular dilatation and hemorrhages. Thus, he concludes that vascular dilatation is due to the effect of mercury on the vasomotor nerves.

To summarize the observations on vascular changes, it is evident that the foregoing list of authorities report as facts more or less constant vascular changes: a rise of blood pressure, first, a fall of blood pressure, later, in some cases not much dilatation; in other cases marked dilatation of all vessels; in still other cases a venous dilatation with arterial constriction. Along with this are many suggestions implicating the vasoneural element as the acting factor in producing these changes, which is altogether probable when the physiology of the nerve control of the blood vascular system is recalled.

Thus, the following passages from Starling [19] suggest that the same picture which we observe in mercury poisoning might possibly be produced by a combination of sympathetic stimulation and gradual asphyxiation.

With both vagi sectioned, "on leaving off the respiration, the blood pressure may remain at the same height for some seconds, the only change noticed being the absence of respiratory oscillations; sooner or later the blood pressure rapidly rises, and in another ten seconds, may reach a height twice as great as it was previously. The heart beats a little more forcibly in consequence of the increased cardiac tension, but its frequency is unaltered. The blood pressure remains at this height for about a minute and then gradually falls, the heart beat becoming smaller and smaller, until the pressure has sunk to a point very little above the abscissa line (level of no pressure). This fall is due to failure of the heart. The heart, badly supplied with oxygen, cannot overcome the resistance presented by the contracted arterioles and hence gets overfilled and gradually loses the power of expelling any of its contents.

"If partial oxygen lack or abnormally increased tension of carbon dioxid be continued for some time, a state of narcosis or paralysis ensues which affects not only the higher centers, but also those of the medulla, so that death may ensue without convulsions or excessive rise of blood pressure.....Oxygen lack may be regarded as synonymous with the production of lactic acid."

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19. Starling: Textbook of Human Physiology, Philadelphia, Lea & Febiger, 1915.

Karvonen [8] reports that Köster, Senger, Lepine, Feitelberg and H. Meyer have all found lactic acid in large quantities in the blood in cases of mercury poisoning.

With the vagi intact, to quote Starling [19] again, "at the point of the tracing corresponding to the rapid rise in the pressure, there is in this case only a slight rise in blood pressure, but the heart begins to beat very slowly. At each beat it necessarily sends out a greater volume of blood than when it is beating more frequently, and hence the oscillations on the blood pressure curve become very large. This slow beat is due to the action of the vagus center and is at once abolished by section of the two vagi."

These references to asphyxiation present in themselves almost sufficient explanation for all the variations of the vascular changes in all the stages and moderations of acute and chronic mercury poisoning in the presence or absence of vagus action. The depletion of red cells, the reduction of hemoglobin in the blood by its combination with mercury, and the presence in the blood of increased lactic acid are certainly sufficient to account for gradual asphyxiation.

When there is added to asphyxiation the probable excitation of the sympathetic system, still further variations of pulse rate, blood pressure and vascular dilatation may be expected.

In many ways, the action of nicotin on the sympathetic ganglions corresponds to the changes we observe in mercury poisoning. On this point, we may also quote Starling: "If the drug be injected, there is an enormous rise of blood pressure, owing to the universal vasoconstriction that is produced. The stimulation gives place to a condition of paralysis; the blood pressure falls below normal, owing to the cutting off of the peripheral vascular nerves from the vasomotor center." This is essentially the same vascular picture we get in mercury poisoning and it suggests that mercury acts similarly on the sympathetic system.

Salivation.—There are other features in mercury poisoning, aside from vascular alterations, which would suggest sympathetic stimulation, such as salivation and glycosuria.

Kaufmann [11] (1888) finds that salivation may or may not be present. Von Mering's dictum, "Stomatitis occurs without ptyalism, and ptyalism occurs without inflammation of the mouth." (Stomatitis ohne Ptyalismus und Ptyalismus ohne Mundentzündung vorkomommt) would indicate that necrosis is independent of ptyalism.[20] The salivation does

20. Cais, J. S.: Mercurial Ptyalism, Nashville J. Med. Surg. **87**:103-111, 1900. Grady, R.: Mercurial Poisoning and Amalgam Fillings; a Medical View; the Dental View, Dental Cosmos **42**:73-80, 1900; ibid., Maryland M. J. **42**:256-260, 1900. Walker, T. J.: Ptyalism Caused by Application of Lotio Hydrarg. Nigra, Brit. M. J. **2**:1146, 1891.

not occur to excrete the mercury since it occurs so shortly after the introduction of the mercury—five or six minutes in some cases.

Oppenheim [21] (1901) reports the presence of mercury in the saliva. The men, he states, who agree with his results are Lehrmann, Kletzinsky, Kussmahl, Heller, Mosler, Salkowsky, Herrman and Wiess;[22] those who negate his findings, Wright, Rostock, Devergie, Warneke, Schneider, Vajda and Paschkis.

Almkvist [23] refers to Kussmahl to the effect that in a chronic mercury stomatitis there is a direct effect on the nerves of the salivary glands and of the colon.

In connection with the nerves to the salivary glands, Starling [19] has this to say: "Thus if the chorda tympani nerve going to the submaxillary gland be cut, no change is evident in the blood vessels of the gland. But if its peripheral end be stimulated, there is instantly free secretion of saliva from the gland, and all the blood vessels are largely dilated. In consequence of this dilatation, the blood rushes through the capillaries so quickly that it has no time to lose much of its oxygen; the blood flowing from the vein is therefore bright arterial in color, and is increased to six or eight times the previous amount. If atropin be injected into the animal, the action of the chorda tympani on the blood vessels is unaffected although the secretion on stimulation is abolished.....Other vasodilators are the small petrosal nerve to the parotid gland and the lingual nerve to the blood vessels of the tongue."

Here, too, the suggestion is that mercury acts on the nerves. In every case, we have vasodilatation of the vessels of the salivary glands, but there may be some action which inhibits the secretion in some cases longer than in others. Going back to the ancient history of mercury, we find that salivation was considered the therapeutic dose of mercury, and physicians continued its administration until salivation resulted. So we know that salivation will result in every case if a sufficient amount of the drug is administered. Its doubtful content of mercury and its sudden appearance in some cases suggest a disturbance of the autonomic element.

Glycosuria.—On this subject we can do no better than review briefly the classic study of Karvonen [8] (1898), from whom the following summary of the related literature was obtained.

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21. Oppenheim, M.: Ueber der Auftreten von Quecksilber im Mundspeichel Arch. f. Dermat. u. Syph. **56**:330-350, 1901.

22. Weiss: The Vicarious Elimination of Mercury Through the Saliva, Clin. Recorder **1**:105-107, 1896.

23. Almkvist, Johann: Om Kvicksilverstomatitis patogens, behandling och prophylax, Hygiea **77**:897-926, 1915.

Glycosuria is a constant finding in mercury poisoning (Saikowsky, Rosenheim, Schröder, Graf); is never present (Balogh, Prevost, Jolles); seldom present (Lazarevic); is irregularly present (Heilborn, Rosenbach). In view of this, Karvonen concludes: (*a*) in severe cases, it always occurs; (*b*) in milder cases, it may not be present; (*c*) in light cases, it is never present.

Graf found sugar, albumin, and quantity changes in the urine to correlate fairly accurately. The excretion of sugar begins a few hours after poisoning, reaches a maximum on the second day, and diminishes to minimal in from four or five to seven days. Schröder reports a maximum in twelve to sixteen hours after poisoning, the maximum being not more than 1 per cent.

Lazarevic investigated hemorrhage in the floor of the fourth ventricle as the cause of this; such was never found, however. Koch's findings speak for a liver diabetes. Glycogen disappears from the liver twenty-four hours after acute poisoning. In a light case, he found glycogen in the liver after three days. The duration of the glycosuria appears to speak for the emptying of the liver as the cause. However, there is no hyperglycemia during the glycosuria (Graf).

It remains to compare mercury glycosuria to phlorizin glycosuria. In every severe poisoning, there is a change in the glomeruli and tubules of the kidneys. Since, however, the sugar content of the blood is not decreased, but insignificantly increased (Karvonen), no dependence can be placed on the liver or nervous system as the source of mercury diabetes.

Although it appears to him, from the recorded observations, that there is no relation of the glycosuria to the nervous system, yet the facts may be interpreted differently. The fact that the liver is completely emptied in severe cases, partially emptied in milder cases and not affected in very mild cases suggests that we have another instance of the action of mercury on the sympathetic system.

It is my impression that the vascular changes, the salivation and the glycosuria are evidences of sympathetic stimulation.

The amount of vascular change depends not so much on the amount of mercury administered as on the individual patient. The vasoconstrictors, due to overexcitation followed by partial paralysis of nerve centers, cause a rise, then a fall, of blood pressure. The tongue and mouth regions are markedly hyperemic because of stimulation of vasodilator nerves. In addition the lack of oxygen creates a tendency toward lack of tonus of vascular musculature, and hence enables any variation or stage of vascular dilatation and weakness to arise.

The salivation, its independence of the ulceration, its questionable function of mercury excretion, its variation in quantity, all point to

the involvement of the sympathetic system, with its variable excitability in different persons.

It is well known that a very severe shock or excitement will cause the liver to lose its glycogen content as a result of stimulation of those nerve centers controlling the liver function. For these reasons, I believe that the entire sympathetic system is activated in mercury poisoning according to the strength of the arousing stimulus and the sensitiveness of the patient.

MOUTH LESIONS

Description of Gross Lesions.—Von Mering [9] and Friedenberg [24] give the following clear, terse, description of the gross lesions: First, there is an appearance of inflammation of the mouth. The mucous membrane of the mouth as well as the gums is swollen. The tongue, swollen, flabby and indented, shows the impress of the teeth; the gums are tender, softened and reddened, and are receded from the roots of the loosened teeth. Edematous pillars of the fauces cause dysphagia,

TABLE 1.—BOCKHARD'S TABLE OF OCCURRENCE

		Occurrence of Cheek Lesion		Occurrence of Gum Lesion	
Patients	Number	Number	Per Cent.	Number	Per Cent.
Men	200	65	32.5	40	20.0
Women	100	44	44.0	28	28.0
Total	300	109	36.3	68	22.7

dribbling of viscid saliva and fetid breath. The inferior maxillary and cervical regions are sensitive to the touch. The teeth are grayish black and tend to caries. On the cheek and the edges of the tongue, there appear grayish-yellow ulcers, marked at the back of the teeth. Ulcers which are irregular, broad rather than deep, show the character of the necrosis.

Causes.—Bockhard [10] (1885) has found a certain order in the appearance of the lesions in which he considered those lesions of the gum and cheek as primary. His table of occurrence is herewith given (Table 1).

Bockhard believes that the saliva contains mercury and its constant flow kills the bacteria. The act of mastication robs certain parts of the gum of epithelium.

Ricord and Bockhard [23] (1885) attributed to the wisdom tooth and its difficult eruption much of the ease with which that portion of the gum is involved in mercury ulceration; as did also Fournier.

24. Friedenberg, A. H.: Hydrogen Dioxide in Mercurial Stomatitis, Am. Med. **5**:129, 1903.

Fournier [25] (1891) classifies the causes of the mercury stomatitis as follows:

1. Of the various forms of mercury administration, rubs of mercury salve cause most stomatitis.

2. Auxiliary causes: (*a*) idiosyncrasy; (*b*)in the mouth itself, the presence of (*a*) infection and carries; (*b*) teeth; in old toothless patients and very young infants, little stomatitis occurs.

3. Predisposing causes: (*a*) sex; more stomatitis occurs in females than in males; (*b*) application of mercury to the genitals or to an open lesion on the skin is inducive to stomatitis.

Lanz [26] (1897) placed no stress on the chemical action of mercury, but he believed that it destroyed nutrition and that the tongue changes were due to the rubbing of the teeth on the tongue. It seems that the teeth make depressions in the tongue, where the ulcers form and from which they spread.

Sklarek [27] (1907) agreed with Bockhard and Lanz that the mechanical injuries of mastication and tongue friction on the teeth are a prime factor in the origin of ulceration following definite tissue change or lack of nutrition (Lanz). The second factor is irritation, in which the action of the mouth and teeth is important. Every stomatitis begins in the socket. An empty socket is not affected. Toothless children and the aged do not have stomatitis. Caries are a big aid and, through the thereby increased pressure on the mucous membrane, increase the local reaction to the stomatitis. The third factor is parasites.

Siebert [28] (1907) noticed also a certain diminished resistance of tissue, which exposes it more to the bacterial action. It is unknown whether there is a specific or mixed infection. Rona's Miller fusiform bacillus answers, especially in the ulcerative forms. Rona found this in pure or almost pure culture in thirty-six cases. While the Miller bacillus is not the first cause, it plays a large rôle in the destructive processes.

Almkvist [29] (1903-1919) attributes to certain bacteria an important rôle under certain conditions. There must be present: (1) albumins broken down by bacteria, thus forming hydrogen sulphid; (2) blood containing mercury.

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25. Fournier, A.: Causes et traitment preventif de la stomatite mercurielle, Méd. mod. **2**:37-39, 1891.

26. Lanz: Klinische und experimentelle Beiträge zur Pathogenese der merkuriellen Stomatitis und Salivation, Berlin, 1897.

27. Sklarek, B.: Ueber die Aetiologie der Stomatitis mercurialis und deren Therapie mittels Pormamint, Berl. klin. Wchnschr. **33**:256-260, 1907.

28. Siebert: Footnote 5, second reference.

29. Almkvist: Footnotes 23 and 28.

Mercury sulphid is formed and deposited in the capillary endothelial cells. Without these two conditions, no ulcerating stomatitis occurs.

A precipitate of questionable composition has long been known.[6] M. Heilborn, in 1878, applied his attention to it. He observed that it was very resistant to ordinary tests and suggested mercuric sulphid. Ten years later, Kaufmann called attention to the same precipitate and attributed to it a large influence on the necrosis. The same year, 1888, Koeniger had found an increase in the black precipitate along lines corresponding to the vessels. The following year, 1889, Falkenberg describes a deposit of black granules in vessel walls and concluded, as Heilborn had previously, that it was probably mercuric sulphid. Marchand wrote a followup on one of Falkenberg's cases and described accurately the necrotic changes and the black pigment precipitate. He believed that the disease of the mucous membrane in place and position is conditioned by the excretion of the mercury.

As for chemistry of the precipitate as claimed by Almkvist it is soluble in tincture of iodid, iodin and potassium iodid solution, and sodium sulphid solution containing sodium hydroxid; insoluble in potassium iodid solution and nitric acid. The precipitate (Almkvist says) always appears before the necrosis. Then, when the karyolysis and phagocytosis begin, the precipitate is carried off with the other débris, so that in late stages one may not see as much of the precipitate as in the early stages. Any localization of mercury poisoning is in a position where there occurs decomposition of albumins. There are certain places attacked primarily and other places secondarily. Unquestionably, the primary attack is in the gum. This is pointed out by most authors. Of all places, the lower gum is most susceptible. The more open the gum cavity, the greater the accumulation and the susceptibility to ulceration.

Leukocytes are present and the epidermis is swollen.[30] Through this swollen tissue, the products are more easily absorbed. The bacteria cannot affect the living tissue; only dead albumin is affected. The hydrogen sulphid is taken up and mercury given off nearest the surface where the capillaries are the smallest. The union of the hydrogen sulphid and the mercury is then a primary step. The precipitation of mercury sulphid which is deposited in the capillary endothelial cells, is harmful from a physical and chemical point of view.

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30. Almkvist: Footnote 23; Ueber die primaren Ursprungstellen und die sekundäre Ausbreitung der merkuriellen ulzerösen Stomatitis und über die Entstehung der Salivation bei Quecksilber behandlung, Dermat. Ztschr. **23**:14-79, 1916; Experimentelle Studien über die Lokalization des Quecksilbervergiftung. Nord. Med. ark. **3**:1-73, 1903.

Other sulphids injected into the tissue will lie dormant like carbon, but mercuric sulphid causes inflammation and may even kill the cells. The second step then is the necrosis of the nuclei and cells. Leukocytic infiltration increases. This offers more surface for bacterial action. Bacteria could not attack the living epithelium, but the dead albumin is a wonderful culture medium.

The third step and final result is a mass of decaying débris, rich in putrefactive bacteria. This spreads laterally and deeply and usually develops quite a large ulcer or slough. One place of special importance is the alveolar socket, where the inflammation dissects down to the periosteum and even extends to the root of the tooth,[31] raising it in its socket, loosening the tooth or even permitting it to fall out. After the process has once started, the mercury does not play such a large rôle: the bacteria do the work.

In some people with dirty mouths, we see changes similar to mercurial stomatitis, but ulceration is not so extensive and it heals more easily. The reason that it heals more easily is that the circulation is not involved and there is not the large mass of epithelium necrosis.

In the tongue, ulceration starts at the depressions. Early, only the periphery of the cup is involved; but Almkvist reasons that, if the tooth pressure causes it, then that part most pressed should ulcerate first; but the brim of the cuplike depression is the first to ulcerate. In some, the whole periphery of the depression is affected. In others, only a part of the periphery is affected. Between the teeth are elevated spicules of gum tissue. The tongue changes are secondary and due to an extension from the gum. Lesions rarely occur on the tongue where no teeth exist.

Almkvist believes that the pterygomandibular fold conceals dead albumin where the lesions can start as already described, spreading from there.

In the tonsils, changes similar to those resulting from administration of mercury may be present without the mercury's having been administered. One of these is the Plaut-Vincent angina. Sometimes these other forms, like the mercury type, show a marked tendency to spread around. Changes may occur in the tonsils without any changes in the gums. Crypts of the lacunae of the tonsils act as the gum

31. Stavely, W. H. C., and Pedley, R. H.: Case of Acute Periostitis of the Jaw from Mercurial Poisoning, Brit.M. J. **1**:889, 1893. Tuthill, J. Y.: Mercurial Necrosis Resulting from Amalgam Fillings, Am. J. Dent. Sc. **23**:97-118, 1899-1900; ibid., Brooklyn M. J. **12**:725-742, 1898. Herzstein, M., and Baer, A. B.: Case of Acute Mercurial Poisoning Followed by General Necrosis of Maxillary Bones and Purulent Otitis Media, California State J. Med. **9**:484, 1911; ibid., J. A. M. A. **58**:854 (March 23) 1912; ibid., Dental Summary **37**:567, 1912.

crypts, and a deposit of foul odor can be picked out as in the gum crypts, with the same bacteria present: *B. fusiformis*, spirilla and cocci.

When the soft and hard palate show changes, there is no primary source except the pterygomandibular folds or the tonsils. After the change has once started, it continues.

Comment.—Gum: I should like to call attention to the important rôle of vasodilatation in causing the gum to become swollen and hence susceptible to the bacteria which are normally present in the mouth, and which take advantage of any débris in the gum crypts to multiply and form hydrogen sulphid with the probable results described. It is, of course, also reasonable to expect that the weakening of the tissue, due to slow metabolism and reduced oxidation (caused by the effect of mercury on the blood and vascular system), exposes the gum more than ever to those influences to which even normal gums succumb. Thus, if infections (pyorrhea, gingivitis or caries) are already present, the organisms have much more favorable circumstances. If infection is not already present, the ulceration and sloughing can be delayed for a time, but eventually a mechanical injury to the vitiated tissues gives rise to an opening infection, which soon spreads rapidly.

Tongue: In the tongue, the importance of vascular changes is still more emphasized; for the dilatation of the vessels is even more marked than in the gums, and no deposit of mercuric sulphid has been reported by those who have studied that fact. However, the swelling of the tongue forces its tissues into the teeth, forming cuplike depressions. It is then conceivable that, as the tongue is moved in the mouth, the ridges of these cups are rubbed against the gums and teeth and the infection already, probably, present in the gums, is transferred to the abrasions thus formed. Probably, Lanz meant that it was the friction of the tongue against the teeth, not the pressure of the tongue on the teeth, which first started the ulceration, since it is the periphery or ridge, not the bowl of the depression, which is first affected. Later, sometimes quite rapidly, the ulceration covers the entire edge and lateral lower surfaces of the tongue.

Cheek: Since the cheek presents its first lesion on a line adjacent to the cutting edges of the teeth, the suggestion is strong that the swollen character of the tissue is an initial factor, for the cheeks would then be pressed closer to the teeth than normally. Even without any change in the structure of the cheek, the mucous membrane may be caught between the teeth and crushed. How much more probable is it, then, that this will occur when the oral mucous membrane and submucous tissues are edematous, infiltrated and hyperemic. The forcing of food between the buccal and alveolar surfaces is an added destructive

agency. Bockhart [10] gives this place as a primary center, while Almkvist [32] takes it to be secondary. According to Almkvist, there is less mercury precipitate here than in the tongue.

Palate: In the palate the same factors hold sway; if infection already is present, this infection will be likely to progress rapidly. If not already present, a longer time will elapse before ulceration begins, and it may not begin at all. Over the palate, we find an extension from the fauces or posterior gum crypts. A palatine ulceration is generally agreed to be secondary.

Specific Organism: It appears to be unknown whether or not there is involved a specific organism. It is more probable that some organism present normally in the oral cavity is permitted by the vitiation of the tissues produced by mercury poisoning to proliferate and thrive at the expense of the body, and the most virulent organism present is likely to be the predominant bacteria.

THE GASTRO-INTESTINAL TRACT

General Clinical Picture.—In a few hours or after a few days, diarrhea occurs. The stools are first watery and are accompanied by active tenesmus; soon, the stools become bloody and extraordinarily abundant; later, almost continual and involuntary. The feces are very fetid. There is violent pain in the rectum and colon. The abdomen is painful and tympantic. There is vertigo and vomiting, with thirst. In some cases, immediately after injection there is severe pain in the abdomen and loins. Later, the diarrhea may stop; as a rule, however, it continues. Sometimes, in severe cases, with the bloody feces is discharged intestinal mucous membrane. If the poison is acquired by mouth, choking and vomiting occur, and pain in the mouth and stomach regions. After one to two hours, there is violent diarrhea with tenesmus.

Gross Lesions.—Ascites: On section, ascites is quite commonly found. The abdominal vessels are constantly filled. Grawitz cut open an experimental animal and observed the action of the mercury at the time of administration. The intestines become congested and the extravasations take place under the mucous membrane, which he attributes to the strong muscular action stimulated by the injected veins.

Stomach: Constantly, in the acute form are found alterations of the stomach and intestines. There is intensive hyperemia, and frequently there are hemorrhagic erosions, most marked in the lower section of the small intestine and upper part of the large, often containing blood-colored content.

In chronic form, the mucous membrane of the stomach and intestine is swelled and is brownish-red to deep gray. Frequently, ulcers occur

32. Almkvist: Footnote 30, third reference.

on the stomach and small intestines. The colon is most affected, and on its folds smaller and larger diphtheritic ulcers occur, which penetrate to the muscle. The stomach contains a greenish content, its folds are edematous with small hemorrhages at their crests. In the cardia and extending toward the duodenum are areas of sprinklings of finely grained, whitish-yellow, of what appears to be exudate but cannot be removed. The stomach at the cardia and pyloris shows multiple punctate hemorrhages, which serve as beginning points for smaller and larger ulcers.

Small Intestine: The jejunum has many folds, greenish-brown and of glassy appearance. The ileum has a very marked hyperemia and numerous tiny hemorrhages.

Colon: The colon in mild poisoning shows a pale mucosa with a few hemorrhages on the crests. Later, there are streaks of superficial necrosis, with scant cloudy gray deposit covering it, firmly attached. The mucous membrane is grayish yellow and strongly swollen, with occasional ulcers with sharply defined borders.

In more severe poisoning, the mucous membrane on the heights of the folds is brownish green and the folds present a polypous comb. The submucosa of the folds is injected with purulent infiltration in patches. Between the folds, the mucous membrane is dark red.

There is a dilating of veins, leading to edema and infiltration of red cells into the tissue—a bloody infarct; and blood in the lumen of the intestine and destruction under the influence of the intestine content. Usually, these changes are very prominent in the beginning of the ascending colon, but not so marked in the appendix or small intestines. The ulceration spreads, infiltrated with leukocytes.

Microscopic Description of Colon.—Marchand [17] has given a very good microscopic description (1891), which is summarized here:

The free edge of the spiral valves of the large intestines is much thickened and dark, and in other places submucous hemorrhages and beginning necrosis occur. The spiral folds consist of a duplicature of the mucous membrane, with an inner muscle. The free edge of the folds are most markedly thickened and hemorrhagic. The swelling consists chiefly of mucous membrane set through with extravasations. Herein one recognizes the remains of the superficial structure. Between the glands are rounded projections which, in the most markedly changed places, are covered and joined by the fibrinous exudate. The superficial tissue takes a poor stain, and the deep tissue is set through with leukocytes whose nuclei stain intensely. The mucous membrane is strongly set off from the submucosa, between the muscularis mucosa and the mucous membrane at the apexes of the strongly changed folds. The submucosa is swollen and, in the areas most affected, infiltrated with

round cells. Between these are the fibrinous and tissue reticulum with enlarged spindle-shaped tissue cells filled with brownish granules. The lymph spaces are obviously dilated and their content contains some cells, the remains of red blood cells. In other places, there are similar lumina filled with red blood cells. Other vessels are dilated. The larger arteries and veins at the border of the musculature are filled with red blood cells. Under the mucous membrane in the walls of the smaller arteries, arterioles, venules and capillaries, can be seen brownish granules which stand out clearly as a regular or irregular network of precipitate. These vessels show stiffness. When cut longitudinally, they present perfectly regular passages which stand out sharply, especially in the center of the necrotic mass. Here and there, between the glands, are spots of clearly traced degeneration and necrosis. The cells are clouded at the height of these crests. The nuclei are pale and indistinct. Here and there, in and between the cells, are darkly stained nuclei—possibly the remains of leukocytes. In other places, the epithelium is entirely brushed away, pushed laterally, jammed together or entirely lacking in streaks. The necrosis and deposit do not necessarily go hand in hand.

In staining for bacteria, many were found in the extensive ulcers, in the exudate and in the lumina of the gland remains. Most of them were the same short bacteria. What the nature of the precipitate is remains unknown, though, beyond doubt, it has to do with the appearance of the mercury in the mucous membrane. The granules exist not only in the necrotic but also in the living tissue where the hydrogen sulphid and the mercury cannot take action.

Marchand thinks that the presence of the mercury in the tissues, as indicated by the granular precipitate, has much to do with the condition. This injurious agent (mercury independent of the precipitate) causes necrosis of the epithelium and superficial vascular membrane. The hemorrhagic and vascular changes are secondary, as is also the precipitate. The tenesmus, as in other dysenteries, is a direct or indirect irritation action through the intestinal nerve endings.

Many other good descriptions have also been made, particularly by Elbe [14] and Weiler,[12] but they have added nothing to that given previously.

Discussion.—From the foregoing description it appears that the intestinal content is delayed longer in the cecum than in any other portion of the intestine. This is interesting in connection with the fact that there is in the cecum a large formation of hydrogen sulphid with a resulting massive deposit of mercuric sulphid, which probably adds to the enervation already initiated by the vasodilatation. Ulceration may, however, occur without the presence of mercuric sulphid, and

certainly marked vasodilatation and submucous hemorrhages can occur without its agency, for mercuric sulphid is not a constant factor. Thus, in the dog's colon and in rabbits fed with oats it does not occur, and yet the lesions appear in each of these. Some more general cause must be involved.

The intestinal muscle contracts violently, crushing tightly filled vessels between muscle and intestinal content. Where bacteria are present, tiny centers of inflammation form on the crests of the folds, which spread in the progress of the lesion to cover large areas of the intestinal wall. Where abrasion of the mucous membrane is absent, large ecchymotic extravasations occur, which may lead to a slough of mucous membrane.

RENAL LESIONS

General Historical Review.—The study of the kidney pathology in mercury poisoning was thoroughly summarized by Karvonen [8] in 1898. Probably no better article has been written since that time. A brief review of his work follows.

Ulrich von Hutten is perhaps the first to have written about anuria as results of mercury. It was undoubtedly a bold advance at his time; and this freethinker had frequent opportunity to observe this condition. The genial Theophrastus Paracelsus observed that the kidney was injured by external application of mercury. The dropsy and cachexia of mercury were also noticed by Paracelsus and other syphilologists of the sixteenth and seventeenth centuries; also the diuretic reaction in cases which lacked salivation (Boerhave, Schlichting, Peter Frank). These views did not prevent the prehunterian physicians from considering syphilis the cause of many dropsy and kidney lesions.

In the first experiment, a monograph by Mathias in 1810, he strongly lays down the hunterian principles. Wells and Blackall, who recognized the relation of albumin and dropsy to kidney disease before Bright, attributed the kidney lesion to mercury. Blackall misconstrued the relation of dropsy and salivation, which he thought occurred simultaneously.

Kletzinski stated that he always found albumin in mercury containing urine, and also often sugar; but his methods were so crude that, of 167 patients to whom mercury had been given, he found mercury in the urine of forty-seven. No wonder he found albumin in the very severe mercury lesions. Overbeck and Kussmahl (1861) say that albumin does not always occur. Frequently, a simple "catarrh" of the urinary organ is produced. Overbeck, in salve cures, produced anuria and found the kidneys enlarged with yellowish fatty cortex. Kussmahl already recognized classic investigation of Pavy (1860), who administered white precipitate by mouth to dogs and cats and produced acute and subacute mercury poisoning. He found the kidneys large and very

much changed, with calcification in the urinary tubules. "The surface was highly speckled. The capsule peeled off, leaving a hard roughened surface underneath in the more advanced specimens. On section, the cortical part was highly striated, consisting, when examined closely, of a number of white columns embedded in the fleshy texture of the organ and running from the medullated part toward the surface. These white columns reaching the surface occasioned the speckled aspect that has been referred to. The uriniferous tubules were displayed, filled with a dark granular matter, the white deposit is of an early character and composed principally of the phosphate of lime. The Malpighian bodies seem to have entirely escaped implication.

"The kidneys are the chief receptacle of the poison (namely, white precipitate), the liver containing a trace, the heart none."

Pavy's beautiful results were repeated in 1866 by Saikowsky. Although animal experiments were often made, yet the kidney was not discussed until after Saikowsky's publication. The next following experimenters discussed chiefly the calcium deposit: Rosenbach, 1868; Balogh, 1875; Heilborn, 1878; Lazarevic, 1879. Prevost, 1879, made investigations from which he concluded that there was decalcification of the bones with the resulting calcification of the urinary tubules. This hypothesis appeared to be strengthened by investigations of Heilborn (1878) and Königer (1888), who found irritation of the bone marrow with increase of the marrow canals. Jablonowsky (1884) and Doleris and Butte (1886) saw increased excretion of calcium and magnesium in urine. This latter finding was negated by Klemperer (1888), who found that the calcium content was certainly often relatively increased, but absolutely always diminished, because oliguria exists. In the blood, then, the calcium content is increased because the calcium excretion through the kidney decreases. Königer's findings were approximately the same.

Kaufmann (1888) established an entirely different theory. He believed that there was coagulation in the capillaries. In this condition, there occurred an anemic (coagulation) necrosis of the kidney epithelium, which attracted calcium from the blood whose calcium content is not increased. Yet no one described later the thromboses described by Kaufmann. Most authors attributed the epithelial degeneration to the circulation or excretion of mercury, as Pavy had done. Leutert (1895) discussed in detail the calcium question, clinically and experimentally. Bergmann (1878), Schide (1884) and Stadfeldt (1884) described cases of poisoning and death in the use of mercuric chlorid as antiseptic at operation. Internal medicine also offered abundant material for study. Jendrassik (1886) had found the diuretic action of mild mercurous chlorid. Investigations were started, in which Welander, Fürbringer and Karvonen figured largely on kidney investigation.

Heilborn,[10] Kaufmann,[11] Weiler[12] and others have given descriptions of the gross character of the lesion, but their descriptions present nothing which does not appear in that of Karvonen.

Mercury is excreted mostly through the urine.[8] It begins to be secreted a few hours after administration, reaches a maximum at the end of the mercury administration and continues, gradually diminishing, for half a year after. Pavy found, on the basis of his experiments, that the kidney takes up more than the liver and the blood.

Ludwig, Zilner and Uhlmann established that the kidney has relatively and absolutely the most mercury of all organs in the body, after which comes the liver, colon, small intestine, stomach, spleen, lungs, heart, etc. This would tend to show that the kidney must have some considerable damage.

The variations of polyuria and salivation are easily explained when one realizes that variations in dispositions of the organs are met with just as are variations in individuals. The kidney and liver are more affected. This is not strange since the kidney is essentially the excretory organ for mercury. Those tissues more susceptible suffer most. Any condition which can add to the already easy susceptibility of the kidney breaks it down that much sooner.

Urine.—Quantity: At first there is an increase (polyuria[33]), later, oliguria.[34] Oliguria or anuria may appear from the start.

Specific Gravity: The specific gravity usually decreases with a rise of quantity and increases with a fall in quantity.

Color: The color is clear, bloody, or cloudy; clear, if the animal is hungry.

Reaction: As a rule, the total acidity diminishes, yet the urine is never so strongly acid that it accounts for the simple precipitation of calcium phosphate, as Kunkel believes.

Albuminuria: This is almost constant, but usually small in amount. Usually, a few hours go by before albumin appears in the urine. During these few hours, polyuria has occurred. If the polyuria continues or passes into oliguria, albumin appears. When healing takes place, the albuminuria gradually disappears. Traces remain for a long time. In severe cases, the urine may never be free again. In men, oliguria is usually accompanied by albumin which quickly disappears in favorable cases. Strikingly, in industrial mercury poisoning, only exceptionally is albumin found (Overbeck, Kussmahl, Streffer, Merget), although cachexia may develop; in medicinal mercury poisoning, albuminuria is

33. Rosenheim: Experimentelles zur Theories der Quecksilberdiurese, Ztschr. f. klin. Med. **14**:170, 1888.

34. Schlayer and Hedinger: Experimentellen Studien über toxische Nephritis, Deutsch. Arch. f. klin. Med. **1**:51, 1907.

often seen. Nevertheless, many syphilologists deny mercury kidney lesions (Fournier, Mauriac, Neumann). In 1892 Lanz said that albumin content in the urine is just as important a symptom of intoxication as infection of the mouth or the intestines. Albumin quantity seldom appears above from 0.5 to 1 per cent.

The manner of origin of the albumin depends not on the arising of the kidney lesion but on the primary alterations of albumin substances in the blood, which becomes more easily dialyzable (Gubler). In acute poisoning, one sees that at least a part of the albumin in the early stages passes through the injured glomerular loops. The presence of nucleoalbumin in the early stages, when the tubular epithelium is just beginning to suffer, speaks for the extraction of the albumin from the cells.

Glycosuria: This has already been discussed under the sympathetic system.

Hematuria: Only in severe poisoning does hematuria occur. The number of blood cells is small, being a simple diapedesis through the glomerular loops. Large hemorrhages are rare. Also the destruction of blood cells in the vessels causes hemoglobinuria.

Gross Lesions.—Vascular filling is an early effect in poisoning; the kidney shows many red points over its surface. Others have also seen intercanalicular extravasations. The veins in the border zone between the cortex and medulla are especially dilated. In a few days, the cortex is swollen and cloudy, pale, gray yellow, or it shows fine white striations and dilated vessels. The medulla is dark reddish brown. After weeks, the kidney appears more normal; but still the cortex is slightly pale and cloudy. Chronic cases show atrophy.

One must examine slides of equal thickness in order to obtain a comparative idea of the amount of precipitate. If one stains with a little picric acid, so that the slide is quite diffusely stained, the granules become yellowish. The convoluted tubules are most affected. The small cells of the loop of Henle are but little affected; the larger cells have some deposit; the collecting tubules show little deposit in the smaller elements, but more in the larger portions.

Microscopic Lesions.—There is strong vascular dilatation of the small veins and glomeruli, beginning changes in the cells of the convoluted tubules. Altmann's granules no longer follow the beautiful arrangement of normality. The affected tubules form in groups from three to six, with faded nuclei and coagulation necrosis; the less affected tubules have, alternately, pyknotic and autolyzed nuclei. The granules, staining black with osmic acid, become larger toward the pyramid. First, there occurs a scattered coagulation of the cytoplasm, with an early cloudy swelling. This undergoes atrophy, with absorption to the bottom. The cells regenerate, therefore, in cases of mild poisoning;

one sees mitoses in some places; in other places diminished, atrophic cells, clear and granule free. In still other places, no atrophic propria and epithelium cells. If the poisoning is more severe, more tubules are involved, until scarcely any remain normal. Repeated small doses leave large or small portions of the kidney normal. This selective island-like necrosis cannot be explained, and leads one to think that all the tubules do not act simultaneously. In acute poisoning, glomeruli are selected.

Calcification: Virchow and Klemperer claim that calcium appears first in the lumen and then in the kidney cells. Others think that calcium appears first in the epithelial cells: 1. Prevost: Calcium deposits in clouded cells whose secretory function is altered. 2. Kaufmann: The coagulation necrotic cell attracts calcium. 3. Virchow: There is calcium metastasis—the calcium content of the blood is too great.

Leutert and Kaufmann agree that calcium originates from the blood or overcalcified urine. These may present a calcium tubule without evidence of protoplasm. Calcification is rare in dogs (Hepp, Grawitz, Heilborn, Aganasiew, Jablonosky). In men, calcification occurs in the convoluted tubules; in rabbits, in the collecting tubules.

Prevost, Köster, Königer, Jablonosky, Kunkel, Virchow, Kobert and von Noorden believe it is a product of decalcification of bone due to mercury. As proof of this, they offer the following facts:

1. There is hyperemia of the bone marrow (Heilborn, Raimond, Königer and Prevost).

2. There is from 4 to 10 per cent. loss of bone weight with increased fragility (Heilborn, Prevost and assistants).

3. The blood contains increased lactic acid which is a decalcifying agent (Feitelberg, H. Meyer, Köster, Senger and Lepine).

4. Calcium and magnesium excretion is increased in the urine (Jablonosky, Bruck and G. Hoppe-Seyler).

In contradiction to this, Heiss says that lactic acid is not decalcifying. Also Königer and Klemperer found no increase of calcium or magnesium in the urine or feces, and they claim that the colon is the excretory organ for these elements.

Finally, Karvonen states that the bones decalcify with hunger. This alone could explain the bone changes in mercury poisoning. G. Hoppe-Seyler found that by absolute rest there is absorption of the bone and the excretion of calcium is increased in the urine. All this shows that the bone atrophy need be no direct result of the mercury.

Fat: Fat is an irregular and variable constituent of the cell.

Pigment: Heinecke found yellow pigment in the kidney. Karvonen found it in a few cases and Leutert found it in one case. It may be blood pigment, but it gives no iron reaction; it gives, however, a little

reaction to Berlin blue. If the kidney is treated with ammonium sulphid, the convoluted tubules present green black granules, which give only in small part the Berlin blue reaction. Others appear black. If the kidney is treated with potassium ferrocyanid and acetic acid, one sees that it is set through with hemoglobin; not only the red cells, but also the hyaline cells, cylinders and granular exudate and many times the necrotic epithelium. In milder cases, only the cylinders and perhaps a few convoluted tubules give this color.

Kobert and Eckmann treated the kidney with ammonium sulphid and other parts with hydrogen sulphid and acetic acid. They could then tell which parts of the precipitate were iron and which mercury. Under the microscope, chemical tests were applied. In the case of mercuric sulphid, there is a fine brown black precipitate lying in the straight tubules of the pyramid. Many tubules show brownish lumina from the mercury secretion.

Cylinders: The homogeneous, finely granular and hyaline are constant. Albumin can be made out on the slide at times. In light cases, when healing is in vogue, desquamation is massive. In chronic cases, the hyalin is more colloidal.

Glomeruli: In the first stages, glomeruli show only blood filling. The loops have become penetrable for blood and albumin. Desquamation and occasional leukocytes occur. Chronic cases show an increase in connective tissue. The vessels are more penetrable, as indicated by dropsy conditions as found by Heilborn, Leutert, Lazarevic and Karvonen. The vessel walls are never thickened. The thrombus formation is not constant and perhaps develops postmortem.

Intersticial Tissue: Provost, von Huber, Steffeck, Weichselbaum, Klein, Leutert and Karvonen noticed interstitial changes. There is an infiltration around the glomeruli, periglomerular small round cell infiltration—only a few polymorphonuclear cells being present. This infiltration leads to an increase of young connective tissue by either mitosis or amitosis. There is a jamming together of squared cells containing nuclei of younger type, which still later gives way to adult connective tissue and finally may wall in the glomeruli and other parenchyma. The vessels show an occasional polymorphonuclear infiltration, but the vascular changes are less marked, with the exception of the glomeruli, which are the same as described in the foregoing.

Comment: Most authors agree with Pavy's explanation of the lesions in the kidney: that the mercury circulating in the blood and being thrown off by the kidney cells injures the cells and renders them partially or totally incapacitated. The presence of mercuric sulphid is an added factor, though not the most important, since there is more

mercury present in the body or any portion of the body than exists as mercuric sulphid. It is probably an indication more of the presence and location of mercury in the kidney than of the injurious element. The larger injury comes from the formation of mercury albuminate with the protoplasm of the cells affected. The peculiar distribution of the lesions has been difficult of explanation, though a significant suggestion has been made by Weiler that the distribution is due to the blood supply. The vessels of the cortex radiate outward from their source in the border zone between the cortex and medulla. This distribution corresponds fairly accurately with that of the lesions, alternating a group of from three to six healthy tubules with a group of from three to six degenerated tubules, showing stages of variation where the one group shades into the other.

In severe cases, all the elements are damaged.

The clogging of the tubules with calcium is the result of the loss of function of the tubules and the natural calcifying processes which the body pursues in an endeavor to heal. The calcium may well be considered a product of the decalcification of the bones, because of inanition due to lack of absorption by the hypermotive alimentary tract and the passivity of the sick animal as Karvonen has suggested.

CONCLUSIONS

From the foregoing literature one would seem justified in drawing the following conslusions:

1. The mercury probably forms a compound with the blood, as indicated by a decreased blood count and by hyperemia of bone marrow.

2. Reduction of oxygen, as a result of the decrease in red cells mentioned in the foregoing and increase in lactic acid in the blood, together with the mercury compound formed, act on the sympathetic system as an irritant, and gradual asphyxiation results, as indicated by vascular changes, salivation and liver glycosuria.

3. Bacteria form hydrogen sulphid in the mouth and colon. This sulphid unites with the mercury in the blood, the mercuric sulphid precipitate being deposited in the capillary endothelial cells, and thus further reduces the vitality of the tissues already injured, independently of the vasodilatation.

4. Bacteria then act on the abrased surfaces of the mouth and colon and form diphtheritic ulcers at those points.

5. The kidney, in an effort to throw off the mercury compounds, probably forms an albuminate from the mercury and the protein of its own functioning cells, which renders these cells less active, the whole process being aided by the disturbed circulation.

6. The idleness enforced by sickness and the inanition produced by poor absorption cause a loss of weight of the bones, with decalcification.

GENERAL COMMENT

It is quite possible, then, from the facts observed by others that the mercury forms a compound with the hemoglobin of the blood, causing a reduction of hemoglobin and a reduction of red blood cells. Vascular changes are produced by the chemical irritation of mercury, and the gradual asphyxiation brought about by the reduced hemoglobin, reduced red cell count, and reduced circulation, and the increase in the lactic acid in the blood presents a stimulus to vasodilators and a stimulus, with later paralysis, to the vasoconstrictors. The result is an initial rise in blood pressure, with later a fall, salivation and glycosuria, which varies according to the excitability of the patient, occurring more frequently in the female. The damming up of the blood in the veins, due to hypotension, permits the arteries to contract about their diminished content.

The pulse rate is usually rapid in severe acute cases and in terminal stages of chronic cases. Otherwise, the pulse rate is slow, probably regulated by the direct or indirect action of the mercury on the vagus or its centers.

Having, then, by all these factors,[35] produced a marked reduction and devitalizing of the tissues, we must take into consideration the action of the bacteria at those points in the body where they most exist. Though, after thorough examination, I failed to observe the mercuric sulphid precipitate described by Almkvist, yet so many competent men have investigated this point that the precipitate is undoubtedly present in some cases and in certain places. Also, it is well known that hydrogen sulphid is very soluble and that mercury and hydrogen sulphid are chemically very active in forming mercuric sulphid, and as we undoubtedly have the two present at the points designated by these authors (the mouth and colon), that precipitate must be an important added factor in the further chemical and mechanical destruction and reduction of those tissues.

The lesions that occur in the mouth can thus be explained by both a general and a specific local action. The findings in the mouth and also other parts of the body, as shown by investigation of the literature, when examined as a whole suggest that mercury has a widespread general systemic effect. These factors having started the process, the mechanical abrasion of the food against the gum and the tongue friction against the teeth, the mucous membrane of the cheek being compressed between the teeth, offer openings for bacteria to make their point of attack.

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35. Almkvist: Footnotes 6, 23, and 30, second and third reference: Almkvist, Johann: Weitere Untersuchungen über die Pathogenese der merkurielle Colitis und Stomatitis, Dermat. Ztschr. **19**:949-1057, 1912.

Similarly, injuries in the intestine (where the hydrogen sulphid is more prominent, and especially in the cecum, where the food is detained for a longer period and where, consequently, mercuric sulphid must be a much more important factor) caused by forcible contractions on the congested veins, as described by Grawitz,[1] give grounds for more bacterial ulceration and proliferation.

One must consider the kidney lesion as being due to the function of that organ in its effort to throw off the toxins in the body. In doing so, the mercury undoubtedly forms an active chemical compound with the protoplasm of kidney cells, thus forming a coagulation necrosis. The selection of the particular cells which we see affected must depend on a number of factors, such as the function of the cell, the chemical activity of the mercurial toxin which a particular cell endeavors to throw off, the vague factors which make up the vitality of the cell and, most important, the blood circulation.[36]

Original Work

Material and Methods

This work was carried on with the research funds of the National Dental Association, under the supervision of Dr. A. T. Henrici, assistant professor of bacteriology at the University of Minnesota, and at the suggestion of Dr. E. T. Bell, professor of pathology, University of Minnesota.

The necropsies and technical work were performed by John Breuer, special technician at the University of Minnesota. To these men, I am, therefore, indebted for the opportunity of obtaining and examining an abundance of material.

In all, thirty-five cats and six ferrets were used. These animals were purchased from an animal supply house; therefore, their history and ages are unknown. They were fed daily from 250 to 500 c.c. of milk, containing from 1 to 5 grains (0.06 to 0.3 cm.) of calomel. At first, the cats were fed milk only, but the last eight or ten animals were fed ground meat once a week. The duration of the poisoning continued from two to ten weeks, producing varying degrees of acute and chronic poisoning. The weight of the animals was tabulated, with few exceptions, once a week, as seen in Table 1. Oral examinations were made every other day and observations noted. Those animals which did not die as a direct result of the mercury action were killed by chloroform. The animals in which lesions appeared portrayed the usual ulcerations around the molar teeth, posterior fauces and cheeks and gums.

The tissues sectioned included practically every organ of the body in some of the animals. The mouth, intestinal and kidney structures

36. Priebatsch: Footnote 2, second reference.

were used in almost all the animals. Tissues were fixed in formaldehyd and Zenker's solution, dehydrated, embedded, sectioned in thicknesses of from 15 to 20 microns, and stained with hematoxylin and eosin. The structures containing bone or teeth were decalcified with hydrochloric acid before being dehydrated. Some special mercury stains were used, as advised by C. Lombardo.[37]

RESULTS

General Clinical Features.—The clinical pictures presented by these animals corresponded in every way to those given in the literature. The gross lesions with their usual variations have been so frequently recorded that an extended description here would add nothing new and would be mere repetition. Only a brief summary of the mouth conditions is, therefore, necessary.

The first thing noted was a paling of the mucous membrane. This color would be changed to a pale bluish or cyanotic appearance, associated with a swelling of the gum, in from one to three weeks. Sometimes this pale discoloration would not disappear until a rather late stage in the poisoning, from five to six weeks. In these cases, the discoloration and collection of tartar and débris around the teeth would assemble before further gum change took place, from two to four weeks after poisoning began, when the teeth would present a heavily coated discoloration. Later, ulceration would occur around the molars, pterygomandibular folds and posterior fauces. The cheeks opposite the alinement of the cutting edges of the teeth displayed a line of ulceration, especially when the gums were ulcerated. The tongue also showed ulceration opposite the teeth, though this did not occur except when the gums opposite were ulcerated. Ulceration of the throat and palate was not observed in any of the cases.

Microscopic Examination.—Internal Organs: Slides of the intestine, kidney, liver and spleen were studied. Changes in these organs corresponded with those recorded in the literature and seemed to vary in no particular from other descriptions as fully reviewed in the foregoing.

Gum: Microscopically, the peridental membrane and the ligamentum circulare dentis are early broken through and destroyed, usually near the tooth. The gum tissue is forced away from the neck, widening the gum crypt, and depressed away from the crown to a considerable extent beyond the normal, sometimes clear to the maxillae, even exposing the bone.

At the point where it should attach, there is necrosis and leukocytic infiltration. The peridental membrane down the sides of the root of the tooth is necrosed to a varying extent, sometimes to the extreme

37. Lombardo, C.: La micro et isto-chimica nella ricerca tossicologicadel mercurio, Arch. di farmacol. Sper. **7**:400-420, 1908.

TABLE 2.—Gross Body Weight of Cats at Various Intervals*

Animal	Weight at Beginning, Gm.	One Week		Two Weeks		Three Weeks		Four Weeks		Five Weeks		Eight Weeks		Ten Weeks	
		Weight, Gm.	Loss or Gain, per Cent.	Weight, Gm.	Loss or Gain, per Cent.	Weight, Gm.	Loss or Gain, per Cent.	Weight, Gm.	Loss or Gain, per Cent.	Weight, Gm.	Loss or Gain, per Cent.	Weight, Gm.	Loss or Gain, per Cent.	Weight, Gm.	Loss or Gain, per Cent.
1	748	890	+19	797	+ 7	.....	....	.....	....	.....	....	.....	....	.....	....
2	525	710	+35	560	+ 7	.....	....	.....	....	.....	....	.....	....	.....	....
3	740	870	+18	711	— 4	.....	....	.....	....	.....	....	.....	....	.....	....
4	586	610	+ 4	.....	....	.....	....	.....	....	.....	....	.....	....	.....	....
5	639	695	+ 9	.....	....	.....	....	.....	....	.....	....	.....	....	.....	....
7	705	790	+12	.....	....	630	—10	.....	....	.....	....	.....	....	.....	....
9	1,400	.....	....	.....	....	.....	....	1,140	—19	.....	....	1,035	—26	911	—35
10	1,425	.....	....	.....	....	.....	....	1,200	—16	.....	....	960	—33	.....	....
12	1,040	.....	....	900	—135	.....	....	.....	....	.....	....	.....	....	.....	....
13	1,210	.....	....	775	—36	.....	....	.....	....	.....	....	.....	....	.....	....
14	970	.....	....	670	—31	.....	....	.....	....	.....	....	.....	....	.....	....
16	1,325	.....	....	1,145	—14	.....	....	925	—30	.....	....	.....	....	.....	....
17	710	.....	....	655	— 7	.....	....	575	—19	451	—36	.....	....	.....	....
18	670	.....	....	580	—13	.....	....	455	—32	417	—38	.....	....	.....	....
20	1,784	1,335	—25	.....	....	1,230	—31	1,315	—26	1,270	—28	1,140	—36	.....	....
21	1,465	1,000	—32	.....	....	818	—44	700	—52	642	—56	.....	....	.....	....
22	1,660	1,530	— 8	.....	....	1,240	—25	1,100	—33	919	—44	775	—59	.....	....
23	2,000	1,808	—96	.....	....	1,300	—35	1,080	—46	915	—54	.....	....	.....	....
24	1,150	1,125	— 2	.....	....	840	—27	635	—45	600	—48	.....	....	.....	....
25	1,180	990	—16	708	—40	.....	....	.....	....	.....	....	.....	....	.....	....
26	1,100	905	—18	790	—28	.....	....	.....	....	.....	....	.....	....	.....	....
27	1,054	1,050	....	990	— 6	.....	....	.....	....	.....	....	.....	....	.....	....
28	1,535	.....	....	1,331	—13	1,245	—19	1,205	—21	.....	....	.....	....	.....	....
29	1,620	.....	....	1,275	—21	1,145	—29	1,000	—38	935	—42	.....	....	.....	....
30	775	730	— 6	728	— 6	775	....	860	+11	915	+18	805	+ 4	740	— 4
31	955	866	— 9	698	—27	614	—36	.....	....	.....	....	.....	....	.....	....
32	1,088	945	—13	745	—32	.....	....	.....	....	.....	....	.....	....	.....	....
33	1,525	1,420	— 7	1,390	— 9	1,445	— 5	1,360	—11	1,410	— 7	.....	....	.....	....
34	1,620	1,590	— 2	1,180	—27	.....	....	.....	....	.....	....	.....	....	.....	....
35	1,270	1,245	— 2	1,050	—17	835	—34	870	—31	.....	....	.....	....	.....	....
36	780	685	—12	605	—22	.....	....	.....	....	.....	....	.....	....	.....	....
37	1,130	1,150	+ 2	1,105	— 2	985	—13	920	—18	.....	....	.....	....	.....	....
38	935	900	— 4	670	—28	.....	....	.....	....	.....	....	.....	....	.....	....
39	720	590	—18	610	—15	.....	....	.....	....	.....	....	.....	....	.....	....
40	900	900	....	730	—19	.....	....	.....	....	.....	....	.....	....	.....	....
41	1,340	1,160	—13	1,230	— 9	.....	....	.....	....	.....	....	.....	....	.....	....
42	1,340	1,260	— 6	1,245	— 7	.....	....	.....	....	.....	....	.....	....	.....	....

* The last weight listed is the weight taken preceding death.

lower limit, or under the root of the tooth. The resulting space is filled with a collection of leukocytes comprising polymorphonuclears and small lymphocytes. The proportions of these types of cells vary.

The necrotic bone spaces in the upper part of the alveolar socket are filled with a similar infiltration. There is perhaps a slight loss of connective tissue also in these places. The gum becomes infiltrated with leukocytes around the ulcers at the apexes of the margins of the gum crypts and on the gum between the teeth. It is here that the lesions first appear. From here, the lesions spread downward, loosening the ligamentum circulare dentis. As the lesions extend deeper and deeper, the peridental membrane finally becomes necrotic throughout its entirety, causing an osteitis even before the entire peridental membrane shows changes. Almkvist also reports the initial lesion to be at the margin of the gum crypt. At times, the entire gum sloughs off to the bone. At other times, the sagging of the gum due to loosening of the ligamentum circulare dentis and the peridental membrane exposes the bone. In these cases, the amount of infiltration is in proportion to the extent of the slough and sometimes becomes very marked.

Tongue: On the tongue, one finds normal mucosa, except for ulcers of different sizes at the junction of the papillary mucous membrane with the lower surface of the tongue and extending under the tongue. The tongue tissue and stroma becomes infiltrated with polymorphonuclear leukocytes and lymphocytes for a short distance around each ulcer. At times, this infiltration becomes extensive. In mild cases, there is no necrosis; there develops a large slough in the more severe cases. As a rule, the vessels are markedly dilated, although in some slides the arterioles are constricted. Many bacteria are found on Gram stain.

Interpretation of Results.—These personal observations, not only on mouth lesions but also on the lesions of other organs, agreeing as they do with the observations reviewed in the foregoing, are not contrary to the idea of the existence of a general systematic effect produced by the mercury. Indeed, as shown in the analysis of the literature, they are best explained as being due to local effects superimposed on more general or widespread changes (in the vascular system, etc.), which make the local lesions possible.

There seems to be no necessity of further enlarging on this idea nor of giving illustrations of the observations, since other authors [34] have fully pictured the lesions, and an extended analysis of their findings has occupied the greater part of this thesis.

Summary

1. In looking up the literature on mercurial stomatitis, I was surprised to find that the explanations advanced for the mouth lesions

were apparently too narrow when all known lesions are taken into consideration.

2. The nine principal theories of the action of mercury on the body are briefly summarized.

3. The essential literature on the pathology of mercury poisoning is analyzed under the system of organs affected, in order to see whether the known facts indicate any general underlying effects which might be involved in local lesions, such as those that occur in the mouth.

4. From the foregoing analysis, it is evident that there are distinct indications of blood and circulatory changes which must be taken into consideration in discussing any local lesion.

5. The results of examining a large number of sections from tissue taken from cats and ferrets with mercury lesions are recorded. These results and their interpretations are fully in harmony with those deducted from an extensive review of the literature.

6. Finally, in connection with the pathogenesis of mercurial stomatitis, I believe that the general systemic action is answerable for the lesions in the same degree as the local changes.

CONCERNING THE SPECIFICITY OF CHOLESTERINIZED ANTIGENS IN THE SEROLOGIC DIAGNOSIS OF SYPHILIS

FOURTH COMMUNICATION *

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Like all other procedures concerned with the treatment or diagnosis of disease, the complement-fixation reaction as applied to the diagnosis of syphilis has been studied extensively, as a result of which the method has experienced decided modifications as compared to the technic originally described by Wassermann, Neisser, Bruck and Detre.

In spite of the large amount of work which has been done, however, we are still in ignorance as to the exact nature of the substance or substances reacting in the test and the mechanism of their production; in fact, as has been summed up by Kolmer,[1] all that is definitely known of the reaction is that while lipoidal extracts (antigens), as well as normal and syphilitic serums, may separately absorb or fix small amounts of complement, a mixture of a suitable extract and a syphilitic serum is capable of fixing large amounts of complement.

If little advance has been made in the attempts to solve the mechanism or modus operandi of the test, great advance has been made in the perfecting of the technical details in order to increase the delicacy of the reaction while maintaining its specificity; and from the investigations which have been made, much information of value has arisen.

COMPLEMENT-FIXATION IN SYPHILIS

The more salient features of the present-day conception of the complement-fixation reaction in syphilis may be thus briefly summed up:

1. The test is not biologically specific and does not represent a true inter-reaction between an antibody and an antigen in a strictly immunologic sense.

2. While the substance or substances reacting may not be true antibodies, at least they are analogous substances, which, until their exact nature is known, are best denominated by the term "reagin."

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* From the Laboratories of The Pittsburgh Hospital.

1. Kolmer, J. A.: Infection, Immunity and Specific Therapy, Ed. 2, Philadelphia, W. B. Saunders Company.

3. The reagin present in syphilitic serums is, in all probability, of a lipoidal nature; whether this results from the biologic or metabolic activities of the spirochetes or from tissue changes or cellular transformations induced by the organisms, is unknown.

4. The "antigens" utilized in the test are not antigens in an immunologic sense, but tissue extracts whose activity and sensitivity depend entirely on the amount and character of their contained lipoids. From this it follows that it is unnecessary that extracts used as antigens be made from spirochete-containing tissues, and, indeed, such extracts are the least delicate of any in use.

5. Because of the nonbiologic character of the test, extracts or suspensions of spirochete cultures are not suitable antigens; and experience has shown that such antigens have feeble and unreliable fixing powers, the fixation that occurs probably being due to the lipoid content of the organism rather than to any combination with a true antibody, though this may perhaps occur.

6. While not a biologically specific reaction, the Wassermann test is relatively specific in a high degree in that the conditions in which nonspecific reactions are usually obtained, such as leprosy, yaws, pneumonia in the febrile stage, and pregnancy when the test is made on the cord blood, are readily differentiated from syphilis.

As far as an actual understanding or explanation of the mechanism of the test is concerned, it must be admitted that the information so far acquired consists mainly of negative knowledge; in the matter of refinement and improvement of technic, in the establishment of more definite knowledge as to its relative specificity, and in the increase of delicacy attained by technical refinements, great advances have been made.

There is still room for improvement, however, particularly in the matter of standardization of technic, so that the test may be performed in a uniform manner, which shall be delicate, specific and reliable in its results. This would permit an impartial and fair comparison of the results obtained by different workers in different laboratories and consequently the accumulation of statistical data in large volume, thus leading to accurate information on many phases of syphilis, such as its incidence, the relative efficiency of various methods of treatment, and the like.

Much study has been given to the matter of standardization, and, a careful trial of a method recently proposed by Kolmer [2] for standard

2. Kolmer, J. A.: A New Complement-Fixation Test for Syphilis Based on the Results of Studies in the Standardization of Technic, Am. J. Syph. **6**:1 (Jan.) 1922.

adoption, the results of which will be published,[3] leads to the conclusion that this phase of the problem has probably been solved.

CORRELATED EFFORTS OF SEROLOGIST AND CLINICIAN NECESSARY TO MAKE DIAGNOSIS OF SYPHILIS

It is regrettable that, to a great extent, the study and investigation of various factors related to and influencing the Wassermann reaction has been more or less relegated to the laboratory, and that it has been mainly on the serologist that the burden of investigating and estimating the value of various modifications of technic has been thrown.

The clinician, in far too many instances, has not interested himself in the matter by coincident clinical or historical investigations, and he has too often been concerned chiefly with critical or even hypercritical censure.

It is in many ways peculiar that while a perceptible proportion of the profession at large are willing to hazard definite and dogmatic statements of diagnostic and prognostic import on the results of Wassermann reactions reported to them, only a relatively small proportion interest themselves sufficiently to acquire at first hand a working knowledge of the theory, principles and technic of the test; of the competence of the worker by whom they permit the test to be made; or of the various factors influencing or modifying the reaction obtained—in a word, to acquire the familiarity with the minutiae of the test necessary to an intelligent interpretation of the results obtained.

There are those who, tacitly at least, seem to assume that it is entirely the duty of the laboratory to make the diagnosis of syphilis; at least, there can be no other assumption tenable when one considers the frequency with which the clinical examination consists of a few perfunctory questions, an equally perfunctory history, and the taking of a specimen of blood, the diagnosis being too often held in abeyance until the report is returned. Far too many persons are being treated for syphilis or dismissed from treatment on the basis of just such a reprehensible procedure. The true number of cases in which the examination for syphilis consists mainly or even solely of a Wassermann test will never be known, but there are grounds for believing that the total would be astounding.

Again, there are others who indignantly refuse to allow the serologist to participate in the diagnosis.

Neither of these attitudes is correct.

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3. Kilduffe, R. A.: The Kolmer Modification of the Wassermann Reaction: A Report of Its Trial in a Series of One Thousand and Fourteen Serums, Arch. Dermat. & Syph. **6**: (Dec.) 1922.

The diagnosis of syphilis, or the determination of the safety and wisdom of the dismissal of a patient from observation and treatment, are matters of great moment not to be hastily decided. In either case the situation is gravid with potentialities of far-reaching importance: mental anguish and distress, physical and mental well-being or destruction, domestic peace or unhappiness; and, often the fate of unborn generations lies in the balance. It is not a question to be influenced by petty manouverings concerned with "professional dignity"; it is rather a question demanding the greatest exercise of professional acumen, experience, judgment and the ability to recognize and evaluate the sum total that alone can make a diagnosis or determine treatment: the history and the physical and laboratory findings, by whomsoever made.

There are certain types of syphilis, such as the latent and hereditary, in which information leading to a diagnosis can be elicited only by the laboratory and the serologist; again, a false or misleading history may be honestly given and the symptoms and clinical findings be so indefinite as to make a clinical diagnosis impossible—such are the borderline cases in which the chance of error is great indeed. In such cases, above all, is it necessary for the clinician and serologist to meet on the neutral ground of consultation, and by a cooperative pooling of their special knowledge to arrive at a proper and intelligent interpretation of their joint findings.

This is just as true of the Wassermann test as a guide to treatment as in the matter of diagnosis—the clinician and serologist should focus their knowledge on the patient together and not separately, as is often the case.

Likewise, in the investigation of matters of technic and the establishment of their true value as affecting the delicacy and specificity of the test, it is not by the efforts of the serologist or clinician alone that the final determination will be achieved; the correlated investigations of both are required.

SPECIFICITY OF CHOLESTERIN-PLUS REACTIONS

Such a question of moment and importance is the determination of the exact status to be accorded to cholesterinized antigens in the serologic diagnosis of syphilis. Because such antigens constitute a permanent part of complement-fixation technic; because they are prominent features in technics proposed for standard adoption, and because there is no uniform agreement as to the frequency with which false and nonspecific fixations may be obtained with them, it is apparently imperative to endeavor to gather sufficient data to decide the degree of specificity to be accorded to cholesterin-plus reactions.

An attempt to arouse interest in this subject and to present data bearing on it has been made in previous communications.[4]

The purpose of the present communication is to summarize the data already presented, with the hope of stimulating a discussion leading to a crystallization of opinion with regard to this question. That this question is of great practical importance is obvious from a consideration of these premises:

If, as has been said, cholesterinized antigens will give nonspecific fixation in a high percentage of normal, nonsyphilitic serums, it is obvious that these antigens should not be used alone in performing the Wassermann test.

Nevertheless, this is the case in numerous laboratories, as has been noted before, and therefore it must be assumed that a certain proportion of normal persons are being classified as syphilitic on the basis of fixations by cholesterinized antigens.

Moreover, two methods of performing the Wassermann test proposed for universal adoption [5] utilize cholesterinized antigens alone, although a new antigen utilized in one technic (Kolmer) is a cholesterinized extract with which is incorporated acetone-insoluble lipoids.

The questions to be investigated, therefore, are:

1. To what extent do cholesterinized antigens react with normal, nonsyphilitic serums?

2. What degree of fixation with a cholesterinized antigen is indicative of the presence of syphilitic reagin?

3. When is a cholesterin-plus reaction indicative of syphilis?

To answer these problems the collection and careful analytic study of a large number of such reactions and their correlation with the clinical findings in the cases concerned is required.

As almost all laboratories include a cholesterinized antigen in their tests and not a few rely on them exclusively, the gathering of such data presents no great difficulty when once started.

As to the superior delicacy of cholesterinized antigens, there is agreement and accord; it is on the question of their specificity that opinion is divided.

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4. Kilduffe, R. A.: Concerning the Specificity of Cholesterinized Antigens in the Serologic Diagnosis of Syphilis, Arch. Dermat. & Syph. **3**:598 (May) 1921; The Specificity of Cholesterinized Antigens in the Serologic Diagnosis of Syphilis, Second Communication, ibid., p. 730. Third Communication, J. Lab. & Clin. Med., to be published.

5. Hinton, W. A.: A Standardized Method of Performing the Wassermann Reaction, Am. J. Syph. **4**:598 (Oct.) 1920. Kolmer, J. A.: A New Complement-Fixation Test for Syphilis Based on the Results of Studies in the Standardization of Technic, ibid. **6**:1 (Jan.) 1922.

The formation of this doubt as to the specificity of cholesterin-plus reactions began shortly after their introduction; and many of the cholesterin-plus reactions then obtained were due largely to a failure to recognize their high antihemolytic power per se and the consequent mal-adjustment of the amboceptor and complement in the system. Also, it must not be overlooked that a certain number of such reactions were undoubtedly due to the presence of syphilitic reagin unrecognized because of the absence of clinical or symptomatic findings.

The lack of clinical evidence played no small part in labeling such reactions as nonspecific.

The points in accord may be thus summarized:

1. Cholesterinized antigens are highly delicate and superior to plain extracts.

2. They will give positive reactions earlier and remain positive longer than plain extracts.

3. The treatment of syphilis should, therefore, be continued until persistent negative reactions are obtained to cholesterinized antigens.

4. Cholesterinized antigens should always be included in complement-fixation technics for the serodiagnosis of syphilis.

In the matter of specificity there is much room for discussion.

It may be admitted at the start that in a certain proportion of normal, nonsyphilitic serums, excluding conditions known to give nonspecific fixation with all antigens, faint (10 per cent.) positive, nonspecific reactions may be obtained with cholesterinized extracts. It is certain, however, that distinct, strong 50 to 100 per cent. fixation occurs much more infrequently than has hitherto been supposed, and there is ample evidence for believing that the phenomenon is, indeed, relatively rare.

That such nonspecific fixation ever occurs in plus four degree is a debatable question and one requiring investigation.

Confusing figures have been published concerning the frequency with which these nonspecific reactions occur, and while in only a few instances the technical details of the tests have been given, it is certain that many of these figures cannot be accepted without question, for several reasons.

Among these may be noted the failure of earlier investigators particularly to appreciate to the full the consequence of a too close adjustment of complement dosage to these antigens of relatively high anticomplementary activities; the failure to use cholesterinized extracts under rigid supervision as to their antigenic or specific inhibitory value; the failure to subject them to extensive and rigorous trial extending over comparatively large numbers of known negatives and positives before placing them in use, and to check constantly their activities by

frequent retitrations. Furthermore, there has been little endeavor to ascertain the exact degree of fixation to be looked on as a frankly positive, specific fixation.

That nonspecific fixation with cholesterinized antigens occurs in 10 per cent. or more of normal cases as a general thing is certainly open to debate; that it ever occurs in plus four degree requires investigation.

The necessity of care in the preparation and standardization of these extracts has been well emphasized by Hinton,[6] who says, after an analysis of 3,701 tests, that: "The percentage of false positive Wassermann reactions must be very small when carefully tested antigens are used."

It may be emphatically disputed that there are justifiable grounds for the attitude not infrequently assumed, which implies or attaches the label of nonspecificity to all cholesterin-plus reactions in general or which necessitates for their specificity a coincident positive history or demonstrable lesion. It is in the doubtful, borderline case without history and without evident, or at most, with indefinite symptoms, that the reaction is often of vital importance, and it is in just such circumstances that its cavalier dismissal as of no significance or value is to be condemned as untenable and unwarranted.

As the problem has been previously stated: Given a serum from a patient with a chancre of five to ten days' standing, a reaction with a cholesterinized extract may frequently be obtained which there is no hesitancy in reporting as a true positive. What is to be the interpretation of such a reaction when the knowledge of the chancre is not at hand?

There is no doubt as to the significance of a cholesterin-plus reaction in a syphilitic patient under treatment; what is to be its significance if the history of treatment is withheld?

Are cholesterin-plus reactions unsupported by historical evidence to be dismissed as without significance, or should they form the starting point of a thorough and exhaustive clinical, historical, and laboratory investigation without which the possibility of syphilis cannot be dismissed? The latter is my contention.

A basis for this contention is found in the work and opinion of numerous other workers, among whom may be noted Graves,[7] who, requiring a plus two fixation for specificity, says: "Cholesterinized antigens did not give false reactions as far as could be ascertained from the clinical data"; Owens,[8] who had 1.5 per cent. of cholesterin-

6. Hinton, W. A.: The Specific Inhibitory Action of Cholesterinized Antigens in the Wassermann Reaction. Am. J. Syph. **5**:1 (Jan.) 1921.

7. Graves, Stuart: The Value of Postmortem Wassermanns, J. A. M. A. **75**:592 (Aug. 28) 1920.

8. Owen, R. G.: Discussion of Graves' paper.

plus reactions in 2,241 tests," all of which were in old, treated cases, some patients having gone as long as fifteen to twenty years without treatment"; McIntyre, North, and McIntyre,[9] who state: "We have never, except in one instance, obtained a reaction using cholesterinized antigens, on any patient on whom the diagnosis of syphilis could not be made, either from the clinical history, the physical findings, or both." And they add that the single exception presents a grave possibility that the patient had had syphilis.

In support of the contention noted in the foregoing, the following summary of cholesterin-plus reactions encountered in over 5,000 Wassermann tests is presented herewith. These cases have been made the subject of previous reports, but they are here gathered into one group.

It must be realized that it was not possible to conduct the investigation systematically, that clinical and historical data were often unobtainable, and that the tests were not made for the purpose of proving or disproving any preformed conception.

The cases reported were simply those occurring in the course of routine examinations. The technic used has been detailed in previous communications, the salient features being the use of a triple antigen battery (cholesterinized extract (0.4 per cent.) human heart, acetone-insoluble lipoids human heart, and alcoholic extract of syphilitic fetal liver), with titrated complement (two units used in the test), two units of amboceptor, an antisheep hemolytic system, and incubation at 37 C. in approximately half the tests, and at 2 to 4 C. in the remainder.

In all, a total of 286 serums reacting to the cholesterinized antigen in plus two to plus four degree—the other antigens being negative—was collected, fixations below plus two being regarded as nonspecific and excluded.

The series presents several points of interest:

First, although a majority of the serums were from a variety of nonsyphilitic conditions, both medical and surgical, cholesterin-plus reactions occurred in only 5.7 per cent. of the total serums examined, thus evidencing that this type of reaction does not occur with undue frequency.

Of the total number of cholesterin-plus reactions, in 127, or 44.4 per cent., a definite history of syphilis was elicited, many being cases of patients under treatment, the extreme interval of infection being thirty-two years previous to the test, this patient having also a plus four spinal fluid reaction and later developing paretic symptoms.

In seven cases a suggestive history was obtained (the wife was a

9. McIntyre, H. D.; North, E. A., and McIntyre, A. P.: Comparative Values of Complement-Fixation Methods in Syphilis, J. Lab. & Clin. Med. **6**:5 (Feb.) 1921.

prostitute; cohabited with a prostitute; the husband or wife had syphilis, etc.). If these were considered as syphilitic, the total of cholesterin-plus reactions shown to indicate syphilis rises to 46 per cent.

These figures, however, include fifty-nine cases in which no historical or clinical data was obtainable, and ninety-three serums of prostitutes in whom, of course, the history was negative, an exhaustive physical examination not being made or, at least, not being reported to the laboratory. In these the possibility of syphilis cannot be dismissed.

In 44 per cent. of 286 cholesterin-plus reactions, therefore, the reaction was shown to be indicative of syphilitic infection beyond cavil or doubt, many being cases in which the serologic finding was the first indication. Had the reaction been looked on as meaningless, 127 syphilitic patients would have been prematurely dismissed from treatment or not treated at all.

In seven cases, syphilis was a strong probability, and in ninety-three it could not be dismissed as a possibility.

Now, however, if we consider the reaction in the 134 cases in which additional data was obtained, we find that in 127, or 94 per cent., syphilis was shown to be present, and the reaction was indicative of the presence of syphilitic reagin. In the remaining seven cases, if syphilis could not be proved, neither could it be denied, the balance of probability being in favor of its presence.

In the face of these findings in conjunction with other evidence heretofore presented, the unqualified dismissal of cholesterin-plus reactions in general is without significance does not seem warranted.

Are we to consider a cholesterin-plus reaction as specific and indicative of syphilis if the patient tells us he has had syphilis—which, after all, may have been pityriasis or ringworm: such things have been made the basis for a diagnosis of syphilis in the past and will be again in the future—or if he tells us that he has never had the disease—truthfully or otherwise—are we to consider the reaction as of no significance?

If the history is to be the sole criterion, the diagnosis rests on a weak prop, indeed.

Or is it to be the clinical evidence that shall decide? What, then, of latent syphilis, of asymptomatic cases, of cases in which the evidence is vague, indefinite, misleading or indecisive?

It is my firm belief that the collection of a sufficiently large series to which can be added complete clinical and historical data, will undoubtedly demonstrate that, with careful and reliable technic, cholesterin-plus reactions in plus two to plus four degree rarely occur in nonsyphilitic serums, if at all, and that such reactions are reliable to a high degree and certainly warrant further investigation before the absence of syphilis can be confidently asserted.

SUMMARY AND CONCLUSIONS

1. Cholesterinized extracts are much more sensitive than alcoholic extracts or acetone-insoluble lipoids as antigens in the performance of complement-fixation reactions in syphilis.

2. Without the use of cholesterinized antigens, either a diagnosis will be missed or treatment prematurely interrupted in a definite and relatively high number of cases.

3. Nonspecific fixation with a carefully titrated cholesterinized antigen is much less frequent than has hitherto been supposed and may be looked on as relatively rare.

4. No syphilitic person should be dismissed from treatment while fixation in any degree can be secured with a cholesterinized antigen.

5. Plus two to plus four fixations with such antigens may be looked on as strongly presumptive evidence of the presence of syphilitic reagin.

6. Cholesterin-plus reactions should not be dismissed in a routine manner as nonspecific, but should form the starting point of an exhaustive clinical and laboratory survey without which the possibility of syphilis cannot be summarily dismissed.

7. A thorough, exhaustive and extensive study of cholesterin-plus reactions is indicated in order that there may be a concerted clinical and laboratory opinion as to their exact status in the serologic diagnosis of syphilis.

CALCIFICATION OF THE SKIN, WITH UNUSUAL FINDINGS

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A review of the literature on calcification and osteoma of the skin suggests two divisions: the first, presenting localized formations such as the case reported by Heidingsfeld,[1] wherein an osteoma, surrounded by a sandy mass, was imbedded in a pigmented nevus. Pusey,[2] in his "Principles and Practice of Dermatology," notes an instance in which an osteoma was found in a keloidal cicatrix, following a laparotomy. Calcification in conjunction with cutaneous neoplasms, such as carcinomas, may be included as examples.

Equally interesting is the second type, characterized by a general distribution of lesions and associated with other pathologic processes of the skin, such as scleroderma and Raynaud's disease, as reported by Hunter,[3] Thibierge,[4] and Haldin Davis;[5] or, the concretions may be formed apparently without being preceded or accompanied by other cutaneous manifestations. It is because of the observations made in a study of the latter, or what may be termed primary, calcification, that the following case is reported.

REPORT OF CASE

History.—Mrs. S., seamstress, aged 50 years, had been subject to so-called "bilious attacks" for the last fifteen years. During this period she had two unusually severe attacks, accompanied by marked epigastric pain and vomiting. There was no jaundice. In July, 1920, following an attack of "asthma" of six months' duration, a concretion the size of a large pea was expelled from the lungs. A similar three weeks' attack in September, 1921, was terminated by the expelling of a concretion approximately one half the size of the first one.

Cutaneous Examination.—This revealed the presence of a hard substance within the skin, assuming a whitish, and at times, a slightly yellowish hue. Single lesions were noted varying in size from that of a pinhead to that of a pea; but the lesions were usually aggregated forming variously sized tumors, the largest having a diameter of 3.5 cm. They were located especially on the

1. Heidingsfeld, M. L.: Osteoma Cutis, Arch. f. Dermat. & Syph. **92**:337, 1908.

2. Pusey, W. A.: The Principles and Practice of Dermatology, New York, 1907, p. 847.

3. Hunter, W. K.: Sclerodermia with Subcutaneous Calcareous Deposits, Glasgow M. J. n. s. **79**:241, 1913.

4. Thibierge, G., and Weissenbach, R. J.: Subcutaneous Calcification and Sclerodermia, Ann. dermat. et Syph. **11**:129-155, 1911.

5. Davis, Haldin: Case of Raynaud's Disease Associated with Calcarious Degeneration, Proc. Roy. Soc. Med., Dermat. Sect. **5**:99, 1912.

extensor surfaces of the left knee, on the left and right elbows and on the proximal phalanx of the left little finger. An unusual site was the extreme tip of the middle finger of the right hand. This accentuated the rôle played by trauma as a thimble was worn continuously on this finger.

Evolution.—The initial lesion had been present for six years. Neither pain nor inflammation was noted preceding or accompanying the appearance of any of the lesions, although once formed, they were naturally subject to pain on pressure. At varying periods, inflammatory reactions supervened accompanied by a softening of the mass and an extrusion of a white paste through sinuses, which, on closing, were followed by scarring. Infection was not demonstrated in association with this process.

Roentgen-ray examination of the chest showed bronchial thickening throughout both lungs, and "calcified" areas were noted at the main stem branches of the upper, middle and lower lobes on the right side, suggesting the origin of the concretions expectorated.

Cholesterol.—Dr. D. A. Tucker of the University of Cincinnati was then asked to investigate the cholesterol content of the blood, by a variation in the fat content of the diet. He found abnormal amounts of cholesterol under all diets, less in the fat-free, more in the normal and still more in a diet rich in fats. At the same time, there was a slight increase in urea with a normal uric acid. His analysis of both the concretions from the skin and lung determined the presence of cholesterol as well as lime.

A later analysis of the blood of the patient by Dr. D. S. Hachen, also of the University of Cincinnati, found the sugar, nonprotein nitrogen, urea, uric acid, creatinin, chlorid (as sodium chlorid) and alkali reserve normal.

Dr. Shiro Tashiro, associate professor of biochemistry of the University of Cincinnati, confirmed the presence of a large amount of cholesterol, plus the lime in the concretions, and made a further analysis of the blood. The results showed that 100 c.c. of the whole blood contained 10.2 mg. of calcium and 0.27 per cent. of cholesterol. A normal calcium content and a slight hypercholesterolemia was thus evident.

From studies on physicochemical conditions accompanying the general process of calcification and on the bile salt, Dr. Tashiro is of the opinion that calcification need not necessarily be preceded or accompanied by an abnormal amount of calcium in the blood, the essential factor for pathologic and normal processes of calcification being the local production of ammonia, or any other base-forming compound, with the normal supply of calcium.[6] This may follow infection, mechanical irritation, or changes in physiologic protein metabolism at the same point.

Similarly, an accumulation of cholesterol in the blood does not in itself necessarily result in a cholesterol deposit in any part of the body. It is Tashiro's opinion that deposition of cholesterol can be occasioned by destruction or removal of the bile salts alone. Such a condition is easily conceivable of production by certain types of infection, since it has been found by Dr. S. Oliver that bile salts are readily destroyed by

6. Tashiro, S.: Am. J. Physiol. **60**:542, 1922.

certain bacteria. His conclusion was, therefore, that the condition, or conditions, necessary for forming such gallstone-like concretions in the skin is analogous to gallstone formation, namely, ammonia production and destruction of bile salts.

In the absence of bacteria, such a condition is highly probable if a local accumulation is such that ammonia production is abnormally high, and cholesterol gradually accumulates to such a point independent of bile salts. In either event, ammonia is generally converted to urea, either in the blood or liver.

ETIOLOGY

A discussion of the various causal theories is not within the scope of this article, but it does not seem presumptuous to state that, in the type of calcification under consideration, a disturbance of metabolism is the essential factor. A particularly pertinent statement was made by J. Bayle [7] as long as eighteen years ago.

> Whatever the cause (irritation, trauma, infection), the vitality of the tissues is altered, and its cells, disturbed in their nitrative functions, perhaps produce substances capable either of precipitating the mineral salts dissolved in the organic fluids which bathes them, or of themselves combining with these same salts to form insoluble compositions.

TREATMENT

Treatment has been and is highly unsatisfactory in the majority of cases, consisting chiefly of surgical intervention. In this case, because of the observation of the decrease of the cholesterol content following the limited consumption of fats, such a regimen has been adhered to. It has been noted that the local accumulation is curtailed by liquefaction and expelling of the contents of the lesions, and this has been artificially duplicated by the application of radium, the smaller lesions being absolutely eradicated and the larger ones materially improved. With these measures, local as well as general improvement has been noted.

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7. Bayle, J.: Study of Calcification of the Skin and of the Subcutaneous Tissue, Paris Thesis, 1904-1905, pp. 9-86.

INSTITUTIONAL EPIDEMICS OF BULLOUS IMPETIGO CONTAGIOSA IN INFANTS*

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Impetigo contagiosa is one of the common skin diseases and, probably because of its usual benign course, the possibility of its occasional virulence is often forgotten. This disease may be divided into four types: (1) the common variety, in which the lesions dry up into a yellowish crust and are readily cured with the proper medicament; (2) the pustular type, in close association with the hair follicle: Bockhart's impetigo; (3) the outbreak of dime-sized lesions, with yellowish brown or brownish crusts and an inflammatory areola: ecthyma, and (4) the bullous type. In the past, the bullous type of impetigo contagiosa has usually been classified as pemphigus neonatorum.

The usual type of impetigo is preeminently a disease of childhood. In a series of 400 cases of this affection seen by Startin (quoted by Crocker [1]), three quarters were in children less than 7 years of age, and only twenty-seven were in adults.

The bullous form of impetigo contagiosa occurs in most instances in infants, and because of its contagiousness is liable to spread through institutions caring for infants. An institutional epidemic of the bullous type of impetigo contagiosa is a serious proposition, as in certain recorded outbreaks the disease has spread like wildfire and has shown a mortality rate as high as 50 per cent.

A review of some of these epidemics will prove instructive. Biddle [2] recorded two epidemics at the Women's Hospital and Infants' Home in Detroit. In one outbreak, his attention was drawn to the occurrence of bleb formations on the bodies of three babies each less than a week old. Within from twenty-four to forty-eight hours, nine other babies in this hospital, three nurses, and two nursing mothers of affected babies were afflicted with the disease. The lesions occurred on the exposed parts of the body in the case of the nurses, the fingers, the ears and the face; and on the nipples and buttocks of the nursing mothers. The eruption in the adult cases was mild, resembling the ordinary type of impetigo contagiosa, and it yielded in the usual course

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* Read before the Philadelphia Pediatric Society, June 13, 1922.

* From the Dermatological Department of the Jefferson Medical College.

1. Crocker: Diseases of the Skin, Ed. 3, 1905, p. 245.
2. Biddle: J. Cutan. Dis., 1914, p. 268.

of time to treatment; but the lesions on the bodies of the babies were extensive, covering in some cases almost the entire surface, and were large, especially over the trunk and buttocks. The constitutional symptoms, high fever, etc., were severe in some of the babies, but no deaths occurred. According to Biddle, the result was not so favorable in an epidemic occurring three years previously in the same institution, in which the mortality rate was 30 per cent., the fatalities occurring within a week or ten days after the onset of the disease.

Schwartz [3] reported an epidemic of this disease in which there were twenty-seven cases in all. Twenty-two developed between the fourth and seventh day after birth and seven patients died, most of them on the fourth to the tenth day of the disease. Cole and Ruh [4] reported an epidemic which occurred in a maternity hospital; there were nine cases with one death.

Hartzell [5] reported a small epidemic in a maternity hospital in Philadelphia, with a mortality of 50 per cent. Knowles [5] recorded an epidemic of thirty cases, with 33 per cent. of deaths, in a public institution in Philadelphia. Pusey [5] reported the occurrence of an epidemic in a maternity ward of one of the hospitals of Chicago, with a mortality rate of 30 per cent. Emma L. Call [5] published an account of an epidemic in the New England Hospital for Women and Children, affecting nineteen infants and three mothers, with a loss of only one infant; this death probably was not traceable to the disease.

Two small epidemics of bullous impetigo contagiosa have recently been observed in the babies' ward in the maternity department of the Presbyterian Hospital and in Dr. Edwin Graham's children's ward at the Jefferson Hospital. Six cases were observed in the first institution and four in the latter.

The cases under our care at the Presbyterian Hospital developed in each baby a few days after birth and the lesions were scattered over the body and the face. Fortunately, there was no mucous membrane involvement or constitutional symptoms of any description, except in one baby who also had multiple abscesses. No deaths resulted.

The four cases observed in infants a few weeks of age, at the Jefferson Hospital, ran a very different course from the series just recorded, as two of the four died. The two patients who succumbed had been operated on by Dr. Warren Davis for hairlip, and unfortunately the operative wound became contaminated with the coccus from one of the other bullous impetigo cases. All four of these cases showed

3. Schwartz: Bull. Lying-In Hosp., New York, June, 1908.

4. Cole, H. N., and Ruh, H. O.: Pemphigoid of the New-Born (Phemphigus Neonatorum), J. A. M. A. **63**:1159 (Oct. 3) 1914.

5. Quoted by Biddle, Footnote 2.

the bullous lesions predominating on the face; the mucous membranes were involved in two of the cases and these terminated fatally.

As to the etiology of impetigo contagiosa, it has long been a mooted question whether the streptococcus or staphylococcus or a combination of the two organisms is causal. Highman [6] states that the cause of the affection is the streptococcus. Such has also been the conclusion of Farley and Knowles [7] in an extensive bacteriologic study of the common type of this affection.

Bacteriologic study of the bullous type of this disease gives a considerably different conclusion. The cases observed by us at the Presbyterian Hospital gave a pure culture of *Staphylococcus pyogenes-aureus*, the material having been obtained from unruptured blebs.

Schwartz studied an epidemic of bullous impetigo contagiosa and found only staphylococci in all cultures made from the blebs, both before and after death. Cole and Ruh isolated *Staphylococcus pyogenes-aureus* in pure culture in all cases in which the fluid from unbroken blebs was obtainable. Pusey believes that the lesions may be produced by different kinds of pus organisms.

It seems logical to us that the different types of lesions of impetigo contagiosa are caused by the different strains or varieties of cocci.

Schwartz thinks "the cause of death may be looked upon as that which has been suggested in cases of burns, namely, as due to induced changes in the red corpuscles or to the formation and absorption of toxic material from the local lesion."

We believe that in those cases in which lesions develop on the lips and extend to the mucous membrane, a fatality usually results from the inability of the infant to take nourishment. In the other cases ending fatally, absorption of the toxic substance from large areas of involvement has apparently been responsible.

Schwartz found nothing especially characteristic beyond slight congestion of the digestive and respiratory tracts and the nervous system in postmortem examinations of cases of bullous impetigo contagiosa.

CONCLUSIONS

Impetigo contagiosa of a bullous type developing in an infant ward is a serious disease and may lead to a high death rate.

It is essential, therefore, immediately to isolate cases of this description developing in an institution containing babies or young children. Every care should be exercised by nurses or attendants handling these cases to avoid further spread of the disease.

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6. Highman, W. J.: Dermatology, New York, Macmillan Company, 1921, p. 261.

7. Farley, D. L., and Knowles, F. C.: Impetigo contagiosa, Arch. Dermat. & Syph. **2**:753 (June) 1921.

THE HISTOPATHOLOGY OF CUTANEOUS TESTS*

SECOND COMMUNICATION

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The clinical significance of a cutaneous test depends on a number of factors, namely: (1) clinical specificity; (2) the employment of a specific irritant, and (3) the production of a specific pathology. Irritants are responsible for histologic changes in tissues and these, in turn, call forth the invasion of certain cellular elements in the tissues affected. In the main, the type of the invading cell determines the general character of the lesion, i. e., polymorphonuclear cells characterize an acute inflammatory process; lymphocytes, mononuclears and endothelial cells, a subacute inflammatory process; and fibroblasts, a chronic process. The phenomena of degeneration, necrosis, etc., are, in the main, associated pathologic occurrences. It is, however, the multiplicity of these various pathologic phenomena and their peculiar localization, together with the presence of definite secondary pathologic changes, that give to a histologic picture a specific character.

While this paper concerns itself primarily with a histologic study of the tuberculin and leutin tests, a brief discussion of both the clinical and anaphylactic status of these reactions would not be amiss. Both tuberculin and luetin tests are considered true anaphylactic phenomena. Roseau and Anderson, as well as others, have observed anaphylactic reactions with various bacteria, such as colon bacillus, typhoid bacillus, anthrax and tubercule bacilli. Indeed, at times, anaphylactic reactions occur during the administration of tuberculin and bacterial vaccines. It is not our purpose to discuss whether or not bacterial toxins are true anaphylactogens, or whether they act by the hypersensitiveness of the body cells for the toxins.

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From the point of view of clinical medicine, the tuberculin (Pirquet) test has an established value; and, subject to certain modifications, some reliance is placed on the luetin test, particularly in the latent, inherited and some obscure phases of syphilis. In view of the status of the tuberculin and luetin tests from the point of view of immunology, and also in view of their clinical significance, we felt that a further contribution to the histopathology of these reactions would be in place.

In a previous contribution [1] relative to the histopathology of positive cutaneous tests, it was stated that the lesion of a positive tuberculin test shows, histologically, a mononuclear cell infiltration in the superficial connective tissue; while the lesion of a positive luetin reaction is characterized by a polymorphonuclear cell infiltration in the deeper connective tissue, together with congestion of the blood vessels and necrosis.

In our present contribution, which embraced seven luetin and two tuberculin reactions, the histopathologic picture was as follows: In the luetin reactions, the predominating features were edema, hemorrhage, congestion and diffuse infiltration with polymorphonuclear leukocytes, particularly involving the deeper layers of the connective tissue; while, in the tuberculin cases, the general character of the cellular reaction was represented by lymphocytic infiltration.

Two factors must be emphasized in this communication: 1. There is a unanimous agreement between the findings in our first contribution and this one, so far as our tuberculin and luetin cases are concerned. 2. In this communication, we have a larger number of luetin reactions to report, namely, seven, and also reactions of various degrees of positiveness. In this paper, the sections were studied by another pathologist (Asnis), who had an open mind on this subject. We can, therefore, present a summary of the histopathology of tuberculin and luetin tests based on the examination of the two pathologists.

Following is a brief summary of the luetin reactions:

REPORT OF TESTS

TEST 1.—The clinical observation was positive. The lesion on the arm consisted of a marked papule about two thirds the size of a bean, with marked surrounding erythema. The lesion was removed for histologic study, with the following report: The superficial connective tissue strata appeared edematous and hemorrhagic. The hemorrhages were rather prominent in the outermost superficial layers of the corium immediately adjoining the stratum Malpighii. The edematous areas were diffusely infiltrated with considerable numbers of polymorphonuclear cells. Lymphocytes were present, but were comparatively few in number. The deeper connective tissue strata presented, in general, the same pathologic process as in the superficial layers, but more intensely accen-

1. Strickler, Albert J.: A Histopathologic Study of Positive Cutaneous Tests, J. A. M. A. **78**:1287 (April 29) 1922.

tuated. The edema was more intense; polymorphonuclear cells appeared in greater number, and in a few areas there were evidences of necrosis.

TEST 2.—There was a positive reaction after forty-eight hours. The lesion was papular, about one half the size of a bean, with erythema. It was removed for histologic study, with the following report: The prominent features of the histologic changes consisted of edema, most intense in the deeper connective tissue structures, and widespread infiltration of polymorphonuclear cells. A moderate number of lymphocytes and an occasional endothelial cell were observed. Small hemorrhages, congestion and degeneration of the polymorphonuclear cells were most evident in the deeper connective tissue layers.

TEST 3.—The clinical result after forty-eight hours was a papule with some beginning pustulation; and very slight erythema (positive). The lesion was removed, and histologically there were noted: considerable hemorrhage and edema throughout the section, and diffuse infiltration of polymorphonuclear leukocytes. In the superficial portion of the corium these cells appeared histologically well preserved; while those present in the deeper layers seemed to have undergone degenerative and necrotic changes.

TEST 4.—The clinical result after forty-eight hours was a papule slightly larger than a pea, with some erythema (weakly positive). The lesion was removed, and histologically there was noted superficial connective tissue infiltrated with a few polymorphonuclears and lymphocytes. The deeper layers appeared edematous and contained a considerable number of polymorphonuclears, not a few of which had apparently undergone disintegration.

TEST 5.—The clinical result was a papule about one half the size of a bean, with surrounding erythema (positive). The lesion was removed; histologically, there were noted: moderate edema and considerable infiltration of cells, the majority of which were polymorphonuclears. There was slight hemorrhage and very little, if any, degeneration of the polymorphonuclears.

TEST 6.—Clinically, after forty-eight hours, there was a papule about two thirds the size of a bean, with marked erythema limited almost entirely to the lesion (positive), which was removed for histologic study, with the following result: The outstanding changes were edema and diffuse infiltration of polymorphonuclears, most evident in the deeper connective tissue layers.

TEST 7.—Clinically, after forty-eight hours, there was a papular lesion surmounted by a pustule with marked erythema (strongly positive). The lesion was removed and histologically there were noted changes occurring largely in the deeper layers of the connective tissue. The pathologic process consisted of considerable hemorrhage, edema, many polymorphonuclear cells, a moderate number of lymphocytes and a few plasma cells.

We can report only two tuberculin reactions:

TEST 8.—Clinically, after twenty-four hours, there was noted an erythematous elevation about one half the size of a finger-nail. The control showed nothing; the tuberculin reaction was positive. The lesion was removed and histologically it was noted that the stratum Malpighii appeared intact. Immediately beneath this layer and extending to the structures of the connective tissue, there were numerous lymphocytes. Some of these cells were diffusely scattered, while others appeared in focal aggregations. In addition, the tissue appeared edematous and the blood vessels were slightly congested.

TEST 9.—Clinically, after twenty-four hours, there was noted at the site of the tuberculin test, a circumscribed elevated papular lesion, with marked surrounding erythema. The control was negative; the tuberculin reaction strongly positive. The lesion was removed for study and histologically there were noted cellular reaction and tissue changes essentially the same as in Test 8, but somewhat greater in intensity. Edema was more marked and was accompanied by small hemorrhages. Lymphocytes were diffusely scattered throughout the section.

With regard to the histopathology of the endermic food reactions studied by us, nothing definite can be stated except that these were not in accord with those obtained in our previous communication and that our present findings were not uniform. We may offer only one possible explanation, and that is that some of our products may have been infected. We hope to repeat this work with fresh material and report in a future communication.

SUMMARY

1. The histopathology of a luetin test based on the study of nine positive results shows a definite and uniform histologic picture which is characterized by polymorphonuclear cell infiltration, the general distribution of these cells being particularly marked in the deeper connective tissues of the skin.

2. The histopathologic picture of a positive tuberculin (Pirquet) test based on four observations of various degrees of positiveness also shows a definite picture; namely, a lymphocytic preponderance in the more superficial connective tissue.

3. We are in no position to offer any explanation for this difference, for in actual diseased states, of both tuberculosis and syphilis, the predominating histologic cell is the lymphocyte.

4. We are doing some research with animals relative to this problem, by means of which we hope to throw some light on the subject of cutaneous tests, which we hope to report in a future communication.

327 South Sixteenth Street.

Abstracts from Current Literature

TWO CASES OF RETINITIS PROLIFERANS OF SYPHILITIC AND DIABETIC ORIGIN. V. L. Raia, Am. J. Ophth. **5**:946 (Dec.) 1922.

These cases were presented to advance the claim that this condition is the result of irritation produced by chemical or toxic substances in the vitreous and not by hemorrhages. The latter is the more commonly accepted view.

OCULAR MANIFESTATIONS IN A CASE OF HYPOPHYSEAL SYPHILIS. F. P. Calhoun, Am. J. Ophth. **5**:952 (Dec.) 1922.

A case of hypopituitarism is reported, with abnormal sugar tolerance, marked choking of the disks and contraction of visual fields, which was unaffected by cranial decompression and by administration of thyroid and pituitary extracts, but responded quickly to antisyphilitic treatment.

HYPOPHYSEAL DISEASE PROBABLY OF SYPHILITIC ORIGIN. B. W. Key, Am. J. Ophth. **5**:956 (Dec.) 1922.

A case is presented with negative syphilitic history, repeatedly negative Wassermann tests, negative spinal fluid, progressive contraction of visual fields, roentgen-ray findings of progressive enlargement of the sella, acromegalic gigantism, external rectus palsy and retinochoroiditis, markedly improved by antisyphilitic treatment, with complete subsidence of marked bilateral choked disk.

H. R. Foerster, Milwaukee.

THE SEMEIOLOGY OF THE PINK DISEASE (ERYTHREDEMA, ACRODYNIA). J. Zahorsky, J. A. M. A. **79**:1975 (Dec. 9) 1922.

Four cases of this disease are reported, with a discussion of the symptomatology. The first symptom is usually a rash, which commonly resembles miliaria. The hands and feet are swollen, dusky red and icy cold to the touch. Irritability, anorexia and leukocytosis are additional features.

THE RELIEF OF PAIN IN HERPES ZOSTER BY PARAFFIN. H. Fox, J. A. M. A. **79**:1979 (Dec. 9) 1922.

Spraying all the cutaneous lesions with paraffin and then covering these areas with a generous layer of absorbent cotton is the method recommended by Fox. The application should be renewed daily after removing the previously applied layer of paraffin.

In three cases of neuralgia following zoster, this treatment failed to give relief.

GUMMA OF THE FOREHEAD WITH RINGWORM: REPORT OF A CASE. H. Goodman, J. A. M. A. **79**:2000 (Dec. 9) 1922.

Scrapings from the lesion revealed spores, and a culture of small spore ringworm was obtained. The Wassermann reaction was strongly positive, and the lesion completely cleared up under specific treatment.

CUTANEOUS ALLERGY IN SYPHILIS, WITH SPECIAL REFERENCE TO THE LUETIN REACTION AND THE NECESSITY FOR CONTROLS IN INTRACUTANEOUS TESTS. J. A. KOLMER and S. S. GREENBAUM, J. A. M. A. **79**:2063 (Dec. 16) 1922.

These investigators employed three products in cutaneous sensitization tests: (1) ascites agar luetin; (2) ascites agar culture medium, and (3) a saline suspension of washed *Spirochaeta pallida*. The results indicate that either true specific cutaneous allergy does not exist in syphilis, or that the cultured spirochetes employed have practically lost their antigenic properties. In syphilis, there is an enhanced nonspecific cutaneous sensitiveness, the origin of which is unknown but which is probably an antiferment adsorption phenomenon.

THE PHARMACOLOGY OF MERCURY. WILLIAM SALANT, J. A. M. A. **79**:2071 (Dec. 16) 1922.

This study is summarized as follows: "Mercury is highly toxic to the heart, causing various cardiac irregularities, such as heart block, delirium cordis and, finally, paralysis. It is also toxic to the respiration, but the effect in this case is not nearly so pronounced as the effect on the circulation. Furthermore, the action of mercuric salts may be greatly increased by citrate or by epinephrin, suggesting that under certain conditions, associated with disturbances of metabolism, the toxicity of mercury may be still more increased."

THE STATUS OF THE NEGATIVE WASSERMANN REACTION. R. A. KILDUFFE, J. A. M. A. **79**:2215 (Dec. 30) 1922.

A negative Wassermann reaction is of value only when intelligently interpreted in conjunction with the other findings; a single negative reaction is of little value in the presence of suggestive clinical findings; and as evidence of cure, a single negative reaction is worthless.

MICHAEL, Houston, Texas.

APPOSITIONAL GROWTH IN CROWN-GALL TUMORS AND IN CANCERS. ERWIN F. SMITH, J. Cancer Res. **7**:1 (Jan.) 1922.

An excellent and comprehensive article is presented, reviewing the theories and present knowledge of mode of cancer growth and reporting experimental studies by the author on tumor and cancer production in the tobacco plant by inoculation with *Bacterium tumefaciens*. The high point in the experiments is the demonstration of conversion of normal cells into tumor cells by contact of the diseased with the normal, that is, by apposition, as against the generally accepted view that cancer grows only by invasion. This altered growth of normal plant tissue is considered due to the irritant action of bacterial infection.

H. R. FOERSTER, Milwaukee.

THE MIXED AND INTERMEDIARY PRICKLE-CELL EPITHELIOMA. J. DARIER and M. FERRAND, Ann. de dermat. et syph. **3**:385 (Aug.-Sept.) 1922.

This peculiar epithelioma, which presents a mixture of the characteristics of the prickle-cell and basal-cell types, clinically as well as histologically, is not

considered rare, having constituted 15 per cent. of the authors' group of prickle-cell epitheliomas. It occurs especially on the face, notably the nose and cheeks, where it may remain stationary for months or years, until it finally starts to grow rapidly, possibly involving the neighboring lymph nodes. It responds less readily to treatment with radium and roentgen rays than does the basal-cell type, and the authors recommend that epitheliomas of the prickle-cell and mixed types be excised if small, or very intensively irradiated if extensive, the prognosis being grave in the latter case.

The article is complete and well illustrated.

FATAL MERCURIAL ERYTHRODERMA FOLLOWING THE INJECTION OF ONE CENTIGRAM OF RED MERCURIC IODID. H. Laborde, Ann. de dermat. et syph. **3**:425 (Aug.-Sept.) 1922.

Although this patient, a woman of 22 years, had also received small amounts of sulpharsphenamin and the bismuth salts, the author feels that the generalized erythroderma and subsequent death were due to an idiosyncrasy to mercury, a small dose of which had been injected intramuscularly. At necropsy, kidney and liver defects were found, of doubtful origin, whose presence may have determined the fatal outcome.

CONSIDERATION OF A CASE OF RECKLINGHAUSEN'S DISEASE. H. Behdget, Ann. de dermat. et syph. **3**:430 (Aug.-Sept.) 1922.

An illustrated description of this disease occurring in a patient apparently the subject of congenital syphilis is presented. The author hopes to stimulate investigation as to the possible relationship between the two conditions.

ISOLATED HYPERALBUMINOSIS OF THE CEREBROSPINAL FLUID IN SYPHILITICS. Cestan and Riser, Ann. de dermat. et syph. **3**:465 (Oct.) 1922.

According to the authors, the presence of increased albumin in the otherwise normal cerebrospinal fluid of syphilitic patients is usually the "scar" from a previous syphilitic meningitis rather than a sign of ill omen. In some of these cases, a "provocative" spinal fluid Wassermann reaction shows a temporary positivity. In certain instances, under treatment, the Wassermann reaction may become negative and the cell count normal, while the hyperalbuminosis persists; and, especially in the "secondary" period, it may also eventually disappear. Illustrative cases are cited.

THE TREATMENT OF LEPRA BY MEANS OF THE SALTS OF THE RARE EARTHS. Noel, Ann. de. dermat. et syph. **3**:475 (Oct.) 1922.

Because of the apparent success of this form of treatment in various forms of tuberculosis, the author has tried its effects, identically administered, in African lepers of various ages, two presenting the macular type and five the tubercular. No simultaneous treatment or hygienic measures were employed. After seven or eight months of this treatment, two cases, one, a tubercular leprosy of nine years' duration, the other of the macular type and present twenty years, showed distinct improvement, with the disappearance of many lesions. The remaining five were not benefited. In view of its apparent occasional success, this form of treatment is suggested as a possible supplement to other measures.

Parkhurst, Toledo, Ohio.

CUTANEOUS GANGRENE OF THE LEG. MILIAN and RIVALIER, Bull. Soc. franç. de dermat. et syph. **29**:231, 1922.

An extensive area of gangrene followed a burn. Cultures were made, and rabbits developed similar lesions at the sites of inoculation. The causative organism, however, was not found.

SYRINGOCYSTOMA IN A DORSAL PLAQUE. HUDELO, OURY and CAILLIAU, Bull. Soc. franç. de dermat. et syph. **29**:235, 1922.

In a child of 3½ years with syringocystoma there was an unusual confluence of the lesions on the right shoulder.

RECKLINGHAUSEN'S DISEASE WITH PSEUDO-ATROPHIC PLAQUES. HUDELO, OURY and CAILLIAU, Bull. Soc. franç. de dermat. et syph. **29**:237, 1922.

These plaques, on a level with the surrounding normal skin, gave the characteristic buttonhole sensation on palpation and were typical of the disease histologically. They are considered as deeper lesions than the usual tumors.

THE TREATMENT OF VICIOUS, ADHERENT AND KELOIDAL SCARS BY IONIZATION WITH POTASSIUM IODID. BOURGUIGNON (JEANSELME), Bull. Soc. franç. de dermat. et syph. **29**:239, 1922.

The terminals were so placed that the current lines traversed the affected parts, and by never exceeding a current strength of from 10 to 15 milliamperes and limiting the treatments to fifteen in a series, favorable results were obtained in severe cases, two of which are cited at length.

THE TREATMENT OF SCLERODERMA BY IONIZATION WITH POTASSIUM IODID. JEANSELME, BOURGUIGNON and LUCAS, Bull. Soc. franç. de dermat. et syph. **29**:247, 1922.

Spurred by their success in the treatment of scars by this means, the authors used the same technic in treating scleroderma in plaques, scleroderma in bands and sclerodactylia, and obtained good results. One case of each type is reported. The discussion is interesting; Darier advises against overenthusiasm, since spontaneous improvement may be seen in this condition.

SCLERODERMA IN PLAQUES WITH DIFFUSE SYMMETRICAL MELANODERMA AND LYMPHOCYTOSIS IN THE CEREBROSPINAL FLUID. LORTAT-JACOB, P. LEGRAIN and E. BAUDOUIN, Bull. Soc. franç. de dermat. et syph. **29**:258, 1922.

The melanoderma, involving the trunk and upper thighs, apparently followed the disappearance of lesions of scleroderma. Little is known about spinal fluid findings in scleroderma. In this case the lymphocytes numbered 16.4 per cubic millimeter, syphilis apparently being absent.

THE TREATMENT OF SEROUS EXUDATION BY OCCLUSIVE ALCOHOLIC DRESSINGS. A. TZANCK, Bull. Soc. franç. de dermat. et syph. **29**:262, 1922.

As a drying agent this application is excellent, and it is recommended for use in localized eczemas.

A DIRECT AND AUTOMATICALLY-LOADING FREEZING CAUTERY. M. VIGNAT, Bull. Soc. franç. de dermat. et syph. **29**:263, 1922.

This apparatus for work with solid carbon dioxid is described in detail. It differs slightly from that described by Lortat-Jacob (see abstract, ARCHIVES DERMATOLOGY AND SYPHILOLOGY **6**:497, 1922).

THE ORGANIZATION OF ANTISYPHILITIC DISPENSARIES. L. QUEYRAT, Bull. Soc. franç. de dermat. et syph. **29**:272, 1922.

Plans are presented for the arrangement and operation of these dispensaries throughout France, the staffs to be appointed after examination. That the patients who come for prophylaxis may not be stigmatized, general medical and surgical cases are also to be handled.

SOME FAILURES OF THE ARSPHENAMINS IN THE TREATMENT OF SYPHILIS. LACAPERE, Bull. Soc. franç. de dermat. et syph. **29**:278, 1922.

The author cites cases in which the use of the brands "neo-arsphenamin," "sulpharsphenamin" and "eparseno" (Ehrlich's "132," for intramuscular injection), as well as the oral administration of oxyaminophenylarsenic acid, has failed, and he comments on the observation that arsphenamin itself seems to be the most reliable, after all.

A CASE OF PAPILLOMATOSIS OF THE BUCCAL MUCOSA. RAYNAUD, MONTPELLIER and A. LACROIX, Bull. Soc. franç. de dermat. et syph. **29**: 281, 1922.

The patient was a native African, aged 22 years, whose skin was free from lesions. It is held that this condition may be peculiar to these natives, possibly being due to their habits of buccal irritation.

GENERALIZED DERMATITIS EXFOLIATIVA OF TUBERCULOUS ORIGIN. M. RAYNAUD, J. MONTPELLIER and A. LACROIX, Bull. Soc. franç. de dermat. et syph. **29**:281, 1922.

In a man, aged 40, who had lately received antisyphilitic treatment, a generalized erythroderma with "eczematoid" patches appeared. At necropsy six months later there was found tuberculous involvement of the lungs, pleura, pericardium and abdominal organs, confirmed histologically, with a microscopic picture of a chronic dermatitis with epidermal and dermal atrophy.

NITRITOID CRISES AND ENDOCRINE TROUBLES. G. LEVY and JUSTER, Bull. Soc. franç. de dermat. et syph. **29**:286, 1922.

Surveying twenty cases, the authors conclude that endocrine disorders are frequent in the subjects of nitritoid crises.

PREVENTIVE TREATMENT OF SYPHILIS. TROISFONTAINES, Bull. Soc. franç. de dermat. et syph. **29**:288, 1922.

Three cases are cited in which the wife, though repeatedly exposed to lesions of the husband, failed to show any clinical sign of syphilis. No mention of serologic examinations is made. It is contended that the women did

not have congenital syphilis. Granted that they were not syphilitic and escaped infection when thus thoroughly exposed, how may we judge the value of the so-called prophylactic treatment of syphilis?

ERYTHRODERMA FOLLOWING TREATMENT WITH ARSPHENAMIN; INTOLERANCE OF ARSENICALS; PERSISTENT SECONDARY LESIONS OF SYPHILIS THROUGHOUT COURSE OF MERCURIAL TREATMENT; EFFECTIVE USE OF TARTROBISMUTHATE OF SODIUM AND POTASSIUM. DECROP and SALLE, Bull. Soc. franç. de dermat. et syph. **29**:290, 1922.

The patient was first seen with a syphilitic chancre of twenty-five days' duration, and the title describes the treatment. This observation emphasizes the fact that the appearance of arsenical erythemas is not a sign of attenuation of syphilitic infection; that in certain cases there is absolute intolerance of arsenical drugs; that mercury, even in high dosage, is too often ineffective; that insufficient treatment merely retards and does not prevent the appearance of secondary syphilitic lesions; that in such cases of intolerance the tartrobismuthate is certainly indicated.

RETRO-AURICULAR GRANULOMA ANNULARE CURED BY APPLICATION OF SOLID CARBON DIOXID. L. DANEL, Bull. Soc. franç. de dermat. et syph. **29**:292, 1922.

In a patient, aged 26 years, there was a lesion 2 cm. in diameter behind the right ear. After two treatments of forty-five seconds each, the lesion disappeared. There had been no biopsy examination.

A CONTRIBUTION TO THE EXPERIMENTAL STUDY OF ZOSTER. G. BLANC and J. CAMINOPETROS, Bull. Soc. franç. de dermat. et syph. **29**: 294, 1922.

In an attempt to check up on the recent experimental controversy, the authors withdrew the contents of vesicles in two cases and inoculated the cornea, conjunctivae and anterior chamber of rabbits, sheep and a pigeon, the skin of rabbits, a monkey and a pigeon, the dura mater of rabbits and the spinal canal of rabbits, a monkey and a dog, with negative or highly questionable results. Further investigations are thought necessary.

THE RÔLE OF BACTERIAL INFECTIONS IN THE GENESIS OF CERTAIN ULCERATIONS WHICH DEVELOP IN LATE RADIODERMATITIDES. L. BROCQ, Bull. Soc. franç. de dermat. et syph. **29**: R. S. 53, 1922.

In the author's opinion, roentgen-ray effects may so modify the tissues as to favor bacterial invasion. Two cases are cited, in one of which there was an unusual amount of necrosis.

BOWEN'S PRECANCEROUS DERMATOSIS. PAUTRIER, Bull. Soc. franç. de dermat. et syph. **29**:R. S. 57, 1922.

In a man, aged 48 years, who had noticed the first lesion twenty years previously, there were many large and small indolent, nonpruritic plaques on the trunk and extremities, including the fingers and the sole of one foot. About fourteen years previously he had been seen by Jadassohn, who had

advised excision of the lesions after a biopsy examination had been made. Pautrier had not yet secured a biopsy specimen, but offered the clinical diagnosis of Bowen's precancerous dermatosis, with possible malignant changes of the lesions of one arm, in which epitrochlear and axillary lymph nodes were palpable. A further report is promised.

TWO CASES OF PRURIGO NODULARIS IN THE SAME FAMILY. PAYENNEVILLE, Bull. Soc. franç. de dermat. et syph. **29**:R. S. 62, 1922.

Mother and daughter presented this condition, and in the latter injections of neo-arsphenamin seemed to diminish the pruritus and to cause the disappearance of some of the nodules. In view of the fact that the mother's eruption had appeared during pregnancy while the daughter's had first been seen at puberty, the author suspects endocrine changes as being causative.

A CASE OF ATYPICAL RECKLINGHAUSEN'S DISEASE. R. SIMON (PAUTRIER), Bull. Soc. franç. de dermat. et syph. **29**:R. S. 66, 1922.

In a young man with skeletal deformities, presenting lesions of Recklinghausen's disease, there was plexiform neuroma and a large tumor of the neck, which, after removal, was diagnosed as arising from the sheath of Schwann (Schwannoma). The epidermis covering this peculiar tumor was deeply pigmented, but no nevus cells were found.

RECKLINGHAUSEN'S DISEASE WITH POLYGLANDULAR INSUFFICIENCY. J. ROEDERER, Bull. Soc. franç. de dermat. et syph. **29**:R. S. 69, 1922.

In a girl, aged 19 years, the condition had been present for five years, accompanied by thyroid hypoplasia and insufficiency with pituitary involvement, while menstrual irregularities suggested ovarian dysfunction. There may also have been suprarenal involvement.

A CASE OF TERTIARY CONGENITAL SYPHILIS OF THE INCISOR TUBERCLE. O. ELIASCHEFF, Bull. Soc. franç. de dermat. et syph. **29**: R. S. 71, 1922.

This condition, recently described by Nicolas (see abstracts, ARCHIVES DERMATOLOGY AND SYPHILOLOGY **6**:499 and 631, 1922), was present in a girl of 10 years. Following the advice of Nicolas, no surgical intervention was made, and antisyphilitic treatment was instituted; sequestra separated and healing ensued.

SYPHILITIC CHANCRE OF THE FOREHEAD WITH A PERICHANCROUS SYPHILOMA. PAUTRIER and ZIMMERLIN, Bull. Soc. franç. de dermat. et syph. **29**:R. S. 73, 1922.

In a man, aged 47, the chancre was of seven weeks' duration, the probable source of contagion having been a wig and mask worn at a fête. The lesion was palm-sized, and a generalized papulosquamous eruption was present.

ADENOGENOUS VENEREAL ULCER. HANNS and WEISS (PAUTRIER), Bull. Soc. franç. de dermat. et syph. **29**:R. S. 77, 1922.

An example of this affection, recently described by Nicolas, appeared in a man, aged 31 years, who had been admitted to the hospital for icterus. One

of his inguinal lymph nodes, at first palpable, soon became enlarged to the size of an orange; it was firm and not very tender. Two small superficial ulcerations then appeared on the penis, and other lymph nodes became palpable. There was some fever. Cultures made from material taken from the large node presented diphtheroid bacilli, probably such as have been previously described. Excision of six of the hypertrophied lymph nodes was followed by apparent cure.

ACANTHOSIS NIGRICANS AND GENERALLY DISSEMINATED PIGMENTARY AND VERRUCOUS NEVI. PAUTRIER and HUGEL, Bull. Soc. franç. de dermat. et syph. **29**:R. S. 81, 1922.

A man, aged 49, presented lesions of forty-four years' duration. He had been shown before the sixth congress of the German Dermatological Society in May, 1898, by Wolff, and his case has been cited by Darier in *La pratique dermatologique* as an instance of the so-called juvenile type of acanthosis nigricans. A detailed description of the lesions is given, illustrated by six excellent photographs, including "close-ups." A histologic report is to follow.

DISSEMINATED MILIARY LUPOID OF THE FACE. PAUTRIER and ROEDERER, Bull. Soc. franç. de dermat. et syph. **29**:R. S. 91, 1922.

A man, aged 29 years, had noticed the first small nodule on the nose two months previously. The involvement soon became extensive. The histologic picture recalled that of hypodermal sarcoid.

A CASE OF LICHEN SCROFULOSORUM WITH THE ELEMENTS IN SHEETS. G. HUGEL, Bull. Soc. franç. de dermat. et syph. **29**:R. S. 93, 1922.

In a man, aged 20, many of the plaques presented an eczematous appearance, so that the identity of the individual lesions was lost.

A CASE OF ATYPICAL EPIDERMOLYSIS BULLOSA. H. MANDEL, Bull. Soc. franç. de dermat. et syph. **29**:R. S. 95, 1922.

In a farmer, aged 46, with no family history of skin disease, localized bulla formation following trauma was first noticed in 1914, the site being the dorsa of the hands. This eruption soon disappeared spontaneously, to reappear in 1921 in the same locations. Nikolsky's sign had been demonstrated, and the characteristic epidermal cysts were present.

GIANT CHANCRE OF THE NECK OF THE UTERUS, SIMULATING EPITHELIOMA. R. SCHEFFER, Bull. Soc. franç. de dermat. et syph. **29**: R. S. 97, 1922.

Twelve weeks after exposure, a woman, aged 48, noticed rather severe vaginal hemorrhage and lumbar pains. *Spirochaeta pallida* was found, and proper treatment instituted.

AN EPIDEMIC OF ONE HUNDRED CASES OF GENERALIZED DERMATOPHYTOSIS DUE TO TRICHOPHYTON GRANULOSUM. PAUTRIER and RIETMAN, Bull. Soc. franç. de dermat. et syph. **29**:R. S. 98, 1922.

Although this organism does not often attack man, the recent German literature contains accounts of similar smaller epidemics (see *Dermat. Wchnschr.*,

1917 and 1919). Two hospitals for the insane and one psychiatric clinic were the foci in the present case, and the authors describe the lesions carefully with the aid of six very good photographs. There were eruptions of three types: (1) generalized and tending to confluence, (2) generalized and consisting of discrete elements, either psoriasiform or vesiculopustular, and (3) simulating ordinary tinea cruris.

SEVEN CASES OF NONSUPPURATING CUTANEOUS PHYTOSES DUE TO TRICHOPHYTON GRANULOSUM. PAUTRIER and RIETMAN, Bull. Soc. franç. de dermat. et syph. **29**:R. S. 109, 1922.

Four of these cases occurred independently of the above-mentioned epidemic.

EXFOLIATING PSORIATIC ERYTHRODERMA. G. MILIAN and LELONG, Bull. Soc. franç. de dermat. et syph. **29**:232, 1922.

This eruption occurred in a man, aged 64, and it was apparently precipitated by two days' exposure to the summer sun and by the application of a tar ointment. A weak chrysarobin ointment was used successfully.

ANTI-SHOCK TREATMENT BY CONCENTRATED GLUCOSE SERUM. R. DUHOT, Rev. belge d'urol. et de dermat.-syph. **5**:1 (Jan.-March) 1922.

A 50 per cent. solution of chemically pure glucose, added to arsphenamin, is said to establish about the arsenical molecule a barrier against the attack of acid mediums, which the author considers to be the cause of nitritoid reactions. He has injected maximum doses of arsphenamin mixed with the glucose solution, in high concentration with no untoward symptoms, and he has even used the acid solution of arsphenamin in doses not exceeding 0.2 gm. Ordinary glucose cannot be used, for it produces toxic symptoms.

MIXING ARSPHENAMIN WITH BLOOD AS A MEANS OF PREVENTING SHOCK: REVINDICATION OF PRIORITY. R. DUHOT, Rev. belge d'urol. et de dermat.-syph. **5**:6 (Jan.-March) 1922.

In May, 1920, the author, at the French Congress in Brussels, announced that reactions could be avoided by aspirating blood into the syringe, where it was allowed to mix with the arsphenamin to be injected. At the Strasbourg Congress, reported in the *Presse médicale* of Oct. 19, 1921, Gastou presented the same suggestion. The author claims priority.

APROPOS AN ARTICLE BY DRS. LESPINNE, LEFEVRE AND POIRIER, ON THE ANTISYPHILITIC DRUGS WHICH CAN BE USED IN THE FIGHT AGAINST VENEREAL DISEASES. R. DUHOT, Rev. belge d'urol. et de dermat.-syph. **5**:9 (Jan.-March) 1922.

The article referred to was read before the Belgian Dermatological Society at the meeting of February, 1922, with a view to the selection of dependable remedies for general use. The author advises against the overevaluation of mercury, stresses the inferiority of sulfarsphenamin, and favors the intramuscular use of amino-arseno-phenol (Ehrlich's "132," called "Eparseno"). He maintains that silver arsphenamin is safe for the use of the general practitioner.

THE TREATMENT OF SYPHILIS BY BISMUTH SALTS. R. DUHOT, Rev. belge d'urol. et de dermat.-syph. **5**:14 (Jan.-March) 1922.

In his recent work, the author has used the tartro-bismuthate of potassium and sodium in oily suspension, given intramuscularly in doses of 0.2 to 0.3 gm. at intervals of four days for as many as six injections in a series. He found that animals tolerated it well, with the exception of some visceral congestion, especially of the kidneys, which followed prolonged treatment. Its intravenous injection is strongly contraindicated. After trying it in all stages of syphilis, Duhot concludes that it is an active drug, second only to the arsphenamins. During its administration the kidneys must be watched, and it is not to be used in cases of nephritis or tuberculosis, nor in ocular syphilis.

THE CHOICE OF ANTISYPHILITIC MEASURES AND THEIR MODE OF ACTION AND APPLICATION; THE PREVENTION OF POST-ARSENICAL REACTIONS. R. DUHOT, Rev. belge d'urol. et de dermat.-syph. **5**:33 (April-June) 1922.

The greater part of this article is devoted to a description of the theory and practice of the author's new method of preventing arsphenamin reactions by injecting the drug mixed with glucose solution. In the author's opinion, the icterus which sometimes appears is usually of infectious origin. The undertreatment of syphilis is condemned, the persistence of foci in the central nervous system being especially cited.

PARKHURST, Toledo, Ohio.

CASE FOR DIAGNOSIS: KERATOSIS FOLLICULARIS SCLEROTISANS. IWANOW and TISCHNENKO, Arch. f. Dermat. u. Syph. **139**:1, 1922.

This article contains the description of a dark oval lesion dotted with brownish red spots which corresponded to corneous plugs in the follicles of the skin. Histologically, there was dilatation and hyperkeratosis of the follicles, and thickening and hardening of the perifollicular connective tissue, with rarefaction of the elastic fibrils. There were no hair or sebaceous glands, while the coil glands were atrophic. The authors suggest the name "keratosis follicularis sclerotisans."

NEW METHODS OF TREATMENT OF TUBERCULOSIS OF THE SKIN AND MUCOSA. WICHMANN, Arch. f. Dermat. u. Syph. **139**:10, 1922.

The author attempted active immunization with material taken from the tuberculous lesions of the patient himself or of another patient. In fifteen of twenty-two cases distinct improvement was seen; in some, surprising benefit

ALTERATIONS OF THE BONE CAUSED BY CONGELATION. PULAY, Arch. f. Dermat. u. Syph. **139**:57, 1922.

Roentgenograms of congelation reveal all degrees of decalcification of the bones, from a hardly visible to a complete decalcification. Decalcification of the phalanges of the third toe and finger are most frequent.

ICHTHYOSIS AS AN HEREDITARY DISEASE. LEVEN, Arch. f. Dermat. u. Syph. **139**:117, 1922.

Ichthyosis vulgaris is essentially different from ichthyosis foetalis. The pedigree of the patients shows that ichthyosis is not limited to either sex.

ELEPHANTIASIS OF THE LABIA. CLINICAL OBSERVATIONS AND PATHOLOGIC ANATOMIC REMARKS. GRAVAGNA, Arch. f. Dermat. u. Syph. **139**:210, 1922.

Gravagna reports a case in which gummatous infiltration beyond doubt caused the beginning and development of elephantiasis of the vulva. No micro-organisms but spirochetes were found. The case proves that in spite of the long duration of the disease the syphilitic infection developed a latent local activity causing an elephantiasis which had so far withstood all arsphenamin medication.

THE PHYSIOLOGY OF ITCHING. ROTHMAN, Arch. f. Dermat. u. Syph. **139**:227, 1922.

Itching represents a weak protopathic pain sensation. If increased, the itching sensation develops into a pronounced protopathic sensation of pain. Scratching displaces the protopathic pain by the epicritic pain.

CHANGES IN THE BLOOD PICTURE IN BALDNESS FOLLOWING GENERAL DISEASES. EICHELBAUM, Arch. f. Dermat. u. Syph. **139**: 235, 1922.

In all cases of symptomatic loss of hair, the author found lymphocytosis, frequently with atypical forms of nuclei. He believes that this lymphocytosis is due to an endocrine disturbance. A typical alteration of the nails was also observed in most patients.

FOLLICULAR CYST AND SPINOUS CELL EPITHELIOMA; NATURE OF SEBACEOUS CYSTS (ATHEROMAS) OF THE HEAD. FREI, Arch. f. Dermat. u. Syph. **139**:269, 1922.

Sebaceous cysts of the hairy scalp histologically resemble epidermoids. Development of carcinoma from a follicular cyst has not yet been described. The author reports a case of sebaceous acne over the whole body, which led to tumor formation on the ear and buttocks. Histologic investigation showed that the tumor had originated from a follicular cyst and had developed into a spinous cell epithelioma with metastases in the neighboring lymph glands.

ACRODERMATITIS CHRONICA ATROPHICANS. JESSNER, Arch. f. Dermat. u. Syph. **139**:294, 1922.

The author reports a case with concomitant xanthoma and fibroxanthosarcoma of the skin without cholesterinemia. Of eight cases examined with the roentgen rays, six showed more or less pronounced atrophy of some of the bones of the acrodermatitic extremities. There were no scleroderma-like alterations. The author believes that a disturbance of the endocrine glands partly accounts for the atrophy.

CHARACTER AND ORIGIN OF PIGMENT OF CHROMATOPHORES IN THE HUMAN SKIN. PHAGOCYTOSIS OF CONNECTIVE TISSUE CELLS. MIESCHER, Arch. f. Dermat. u. Syph. **139**:313, 1922.

Careful experiments confirm the fact that connective tissue cells possess the capacity to absorb soluble and insoluble substances from the tissue fluid and to store them. This refers both to chemically indifferent substances, such

as india ink and cinnabar, and to such substances as melanin. Furthermore, as it was possible to create chromatophores in the corium by injecting melanin, the author is convinced that the pigment cells found in the corium represent chromatophores which have taken up the pigment they derived from the epidermis. The cells of the epidermis cannot retain pigment probably on account of some damaging factor or degenerative alteration. Whether the pigment leaves the cell in a soluble form or as a grain of pigment is not known. Even the normal epidermis shows a certain degree of incapacity. Some skins, however, in spite of deep pigmenattion, do not possess any chromatophores, or hardly any. The author believes that the transference of pigment to the cutis is a pathologic process.

THE CLINICAL VALUE OF THE COLLOIDAL GOLD REACTION IN SYPHILITIC LIQUOR CEREBROSPINALIS. GRÜTZ, Arch. f. Dermat. u. Syph. **139**:426, 1922.

The author believes that a colloidal chemical reaction is essential for a reliable spinal fluid diagnosis. The colloidal gold reaction is the most important and is superior to the mastic reaction.

A HITHERTO UNDESCRIBED FORM OF NEVUS (COBBLE STONE SHAPED CONNECTIVE TISSUE NEVUS). LIPSCHÜTZ, Arch. f. Dermat. u. Syph. **139**:447, 1922.

This is a report of four cases showing a mosaic-like picture of polygonal nodular eruptions on the trunk, which histologically had the character of a connective tissue nevus.

AORTITIS LUICA. SCHITTENHELM, Deutsch. med. Wchnschr. **48**:60, 1922.

The author calls attention to the danger of overlooking an aortitis, as even the best roentgen-ray technic cannot always assure one of a correct diagnosis. A hidden syphilitic involvement of the aorta is frequent. The author treats syphilitic aortitis with a total dose of 4.5 to 6 gm. of neo-arsphenamin combined with inunction treatment; he also recommends the permanent treatment method of Schottmüller.

THE DISTRIBUTION OF LEUKOCYTES IN THE BLOOD. STAHL, Deutsch. med. Wchnschr. **48**:314, 1922.

The number of leukocytes in the capillaries of the skin is a little larger than the number in the larger vessels.

A PRACTICAL METHOD OF DETERMINING DOSAGE OF ALPINE SUN LIGHT. KELLER, Deutsch. med. Wchnschr. **48**:346, 1922.

The following method is useful for measuring an Alpine sun erythema dose (A. S. E.) also for testing the efficiency of old and new lamps: A tumbler, 5 c.c. in diameter with 100 c.c. capacity is filled with 2.5 c.c. of a 1 per cent. potassium iodid solution, 25 c.c. of 5.3 per cent. sulphuric acid, from 6 to 8 drops of a 1 per cent. starch solution and 1 c.c. of 400th-normal sodium thiosulphate solution. This solution is placed within half the therapeutic exposing distance and left until it turns bluish. The time required is the Alpine sun unit.

IS MERCURY A SYMPTOMATIC AGENT OR DOES IT INFLUENCE THE COURSE OF SYPHILIS? HELLER, Klin. Wchnschr. **1**:519, 1922.

Contrary to Lesser, the author believes that mercury is not only a symptomatic agent, but that it has a decidedly beneficial influence on the course of the disease. Statistics gathered in Russia, Bosnia, Herzegovina and Anatolia on a large number of patients who had been treated with mercury only prove that mercury prevents the development of tertiary symptoms.

INFLAMMATION, ALLERGIC IMMUNITY AND ANAPHYLAXIS. KLINKERT, Klin. Wchnschr. **1**:680, 1922.

The author believes that anaphylaxis, allergy and inflammation are identical biologic processes. For example, he believes that an attack of gout is an angioneurotic inflammation and considers it analogous to anaphylaxis.

THE TREATMENT OF SOFT CHANCRE. BRUCK, Klin. Wchnschr. **1**: 689, 1922.

Auto-inoculation enables one to make the safest diagnosis. The author recommends nonsyphilitic parenteral protein treatment of buboes. Immunization with a streptobacilli vaccine gave good results, although the preparation of the vaccine was difficult.

A NOTE ON THE SEXUALITY IN SPORADIC CRETINISM. WOLLENBERG, Med. Klin. **18**:144, 1922.

Myxedema is generally combined with disturbance of the genital system. The author discusses a case of pronounced infantile myxedema which, in spite of all typical symptoms, showed perfectly normal genital functions.

PRACTICAL EXPERIMENTS IN DIAGNOSIS WITH CONGORUBIN. GUTFELD and WEIGERT, Med. Klin. **18**:148, 1922.

The aqueous 1:1,000 congorubin stain solution resembles the colloidal gold solution. The authors add 750th-normal hydrochlorid acid to change the color from red to blue. Dilutions of spinal fluid of 1:20 prevent change of color. In the thirty-eight spinal fluids examined this way, fifteen reactions corresponded to the colloidal gold reaction. The technic needs improvement. As yet this method has no practical value.

PITYRIASIS ROSEA IN SYPHILITIC PATIENTS, WITH REFERENCE TO THE JARISCH-HERXHEIMER REACTION. FEIT, Med. Klin. **18**:209, 1922.

The author observed a distinct Herxheimer reaction on pityriasis rosea lesions in a case of secondary and also in a case of tertiary syphilis following mercury or arsphenamin injections. The Herxheimer reaction is not specific, though a definite explanation has not yet been given.

TURBIDITY FLOCCULATION REACTION. DOLD, Med. Klin. **18**:212, 1922.

Syphilitic serums cause a flocculation of the lipoid extracts. While hitherto attention has generally been directed to the final stage of this process, Dold assumes that syphilitic serum precipitates the extract lipoids at the very

moment serum and extract make a contact, the process thus passing an early preliminary colloidal, finely dispersed stage before forming the large flocculae in the Sachs-Georgi and Meinicke reactions. Dold's method tends to render macroscopically visible the early colloidal stage of this process.

LIGHT ERYTHEMA AND WAVE LENGTH. Axmann, Med. Klin. **18**: 216, 1922.

The rays between 302 and 297 microns cause erythema and pigmentation. It is therefore of fundamental importance to increase this sphere in the lamps (Alpine sun, etc.) used, and not to lengthen the spectrum.

CASE OF ARSENICAL POLYNEURITIS. Cohn, Med. Klin. **18**:371, 1922.

The administration of 100 gm. of a solution of potassium arsenite (Fowler's solution) within six months caused polyneuritis in a psoriatic patient in the form of paresthesia in the legs, while the skin lesions regressed. Four months later, the patient developed extensive erythrokeratoderma, also melanosis and hypertrophy of the skin of the feet and hands. The disturbances were due to chronic arsenic poisoning.

THE STAINING OF COLLOIDS FOR SEROLOGIC EXAMINATIONS. Hecht, Med. Klin. **18**:439, 1922.

The author describes experiments with stains to render flocculae more clearly visible in flocculation reactions. Sudan, gentian violet and methyl green pyronin proved useful in the Hecht and Sachs-Georgi reactions. Similar experiments with the Wassermann reaction gave no results.

PITYRIASIS ROSEA IN A CHILD AGED ONE YEAR AND NINE MONTHS. Leiner, Mitt. d. Gesellsch. f. inn. Med. u. Kinderheilk. **20**: 25, 1921.

This is the report of a case which was cured by one intramuscular injection of a milk protein.

SKIN AND MUCOSA HEMORRHAGE WITH BONE MARROW DAMAGE AND DEATH FOLLOWING ARSPHENAMIN-MERCURY-COLLARGOL TREATMENT IN SECONDARY SYPHILIS. Vill, München med. Wchnschr. **68**:52, 1921.

The author warns against administration of collargol intravenously during or shortly after mercury-arsphenamin treatment.

CONTRIBUTION TO THE CLINIC OF MERCURIAL ERUPTIONS. Wolf, München. med. Wchnschr. **68**:52, 1921.

A description is given of a rash caused by an amalgam filling in a tooth.

ARTIFICIAL LIGHT THERAPY. AN "IRRADIATION-CHAMBER" FOR SOURCES OF ARTIFICIAL LIGHT. Picard, München. med. Wchnschr. **68**:1142, 1921.

The therapeutic effect of artificial light can be considerably increased by using a chamber the walls of which are covered with a reflecting layer of

aluminum. Theoretically, the author believes that the effect of rays of light on the body are due to the hemoglobin of the blood, which contains metal, and which thereby transforms the energy of the rays.

PROTEIN BODY THERAPY. Weichardt, München. med. Wchnschr. **69**: 107, 1922.

Activation of the protoplasm does not always cause stimulation. There are circumstances under which activation does not result in stimulation but in the paralyzing of the body cell.

THE PSYCHOGENIC CONSTITUENTS OF PRURITUS AND PRURIGINOUS DERMATOSES. Sack, München. med. Wchnschr. **69**:148, 1922.

The author distinguishes three groups (1) psychogenic pruritus without skin alterations; (2) psychogenic pruritus with skin alterations, and (3) pruriginous dermatoses with psychogenically increased irritability. Therapeutically suggestive measures (hypnosis) gave satisfactory results.

THE TREATMENT OF CHILBLAINS AND CHRONIC FROSTBITE WITH THYROID EXTRACTS. Embden, München. med. Wchnschr. **69**: 201, 1922.

The therapeutic effect is said to be due to the influence on the damaged vessels. The effect was not reliable clinically.

PARENTERAL TREATMENT WITH NONSPECIFIC ALBUMIN BODIES. Stintzing, München. med. Wchnschr. **69**:229, 1922.

We still lack definite knowledge of nonspecific protein treatment. No hard and fast rules can yet be laid down as to dosage, indication and choice of protein in a particular case.

NEO-SILVER ARSPHENAMIN IN NEUROSYPHILIS. Dreyfus, München. med. Wchnschr. **69**:268, 1922.

Report is made of 5,000 injections. The effect is not quite so strong as that of the same dose of silver arsphenamin. However, it is stronger than the arsphenamin preparations which are not combined with silver. Neoarsphenamin is very stable in the air, showing no signs of decomposition after exposure for from one to six hours. This is one of its main advantages.

CONTAGIOUSNESS OF CONDYLOMA ACUMINATUM. Lichtenstein, München. med. Wchnschr. **69**:270, 1922.

Report is made of a case which induced the author to believe venereal warts to be contagious.

TREATMENT OF TUBERCULOSIS WITH ROENTGEN RAYS. Hilpert, München. med. Wchnschr. **69**:348, 1922.

In tuberculosis of the skin the author exposes the skin to one erythema dose of roentgen rays under 0.5 mm. of zinc per field and repeats this treat-

ment two or three times every six weeks. In superficial lupus only the lesions were exposed to an erythema dose under 3 mm. of aluminum; the dose was repeated after six weeks. Excellent results were obtained.

MIXING OF PREPARATIONS OF MERCURY AND ARSPHENAMIN AND THEIR THERAPEUTIC APPLICATION. Bothman, München. med. Wchnschr. **69**:427, 1922.

The author reports 242 cases treated with a mixture of arsphenamin and mercuric chlorid in one syringe. The author believes that this mixture is therapeutically less efficacious than the administration of each drug separately.

PROPHYLAXIS AND TREATMENT OF TABES AND PROGRESSIVE PARALYSIS WITH QUININ. Adler, Psychiat.-neurol. Wchnschr. **23**: 279, 1922.

The author advises prolonged quinin medication in the treatment of tabes. However, as the spirocheticide effect in vitro does not correspond to the chemotherapeutic effect in the system, and as the inefficiency of quinin medication in syphilis has long been proved, the author's suggestions are of little value.

ON THE PATHOGENESIS OF TABES. Richter, Schweiz. Arch. f. Neurol. u. Psychiat. **9**:65, 1921.

Richter traces the beginning of a tabetic process to Nageotte's point. He discovered a curious granulation tissue at this point, with *Spirochaetae pallidae*.

NECROSES OF SUBCUTANEOUS FAT-TISSUE IN NEW-BORN CHILDREN. Bernheim-Karrer, Schweiz. med. Wchnschr. **52**:12, 1922.

This is a report of five cases of so-called scleroderma neonatorum. All cases showed infiltrations in the deep skin layers. The nodules generally developed from the seventh to twentieth day. There was no scar formation, as the resorption was rapid. This disorder has received little attention. The author believes that the lesions are due to trauma (pressure of forceps) during labor. Histologically, the condition is characterized by a circumscribed involvement of the subcutaneous fat-tissue causing necrosis. Hence the scleroderma of the new-born clinically and histologically differs from genuine scleroderma.

THE STIMULATION AND PARALIZATION OF ANIMAL CELLS THROUGH ROENTGEN-RAY EXPERIMENTS ON FROG EGGS AND LARVAE. Hoffmann, Strahlentherapie **13**:285, 1922.

From one fifth to two fifths of an erythema dose decidedly hastened development, growth and metabolism of frog larvae, while doses larger than two fifths inhibited growth.

Ahlswede, Hamburg, Germany.

Society Transactions

PHILADELPHIA DERMATOLOGICAL SOCIETY

Regular Meeting, Nov. 13, 1922.

FRED WEIDMAN, M.D., *Presiding*

CHRONIC URTICARIA. Presented by DR. MUNSON.

A woman, aged 30, had had the disease for two years. Food tests as well as bacterial protein tests were negative.

DISCUSSION

DR. KNOWLES said that the symptoms in this case were controlled by the administration of thyroid extract.

DR. SCHAMBERG cited a case of his that had been caused by shock.

LUPUS ERYTHEMATOSUS DISSEMINATUS. Presented by DR. SCHAMBERG.

The two cases presented showed a parallelism of symptoms. Both patients were women, about 20 years of age, and showed characteristic lesions located on the dorsa of the hands, on the chest, face and scalp. One patient had had a sinus infection for four years. This was followed by an acute and then a chronic nephritis. Treatment consisted of rest, forced feeding and the administration of 1 grain iodoform pills, three times a day. One patient showed a marked increase in weight, and convalescence was correspondingly more advanced.

DISCUSSION

DR. STOKES discussed the cases. He said that during the last two years he had seen nine cases paralleling these; three of these came to necropsy, and two showed mesenteric tuberculosis. He suggested deep roentgen-ray therapy directed to the lymphatic system. He cited the case of one patient treated over a period of two years who was now free from symptoms. He regarded it as possibly a toxic erythema incident on a staphylococcic invader on a tuberculous allergic base. Discoid and disseminate types represent different phases of the same phenomena.

LUPUS VULGARIS. Presented by DR. SCHAMBERG.

A colored youth, aged 17, had had lupus vulgaris for thirteen years, and the parts involved were the nose, upper lip, right side of the face and the right eyelid. The patient was being treated with a 25 per cent. pyrogallic acid cerate. Dr. Schamberg said that the ulcerative type gave good results with roentgen-ray therapy, but that the nonulcerative type gave negative results. He said, further, that if the patients did not show prompt improvement under roentgen-ray treatment, it was to be discontinued.

DISCUSSION

Dr. Knowles spoke of the great number of patients being treated in Darier's clinic, St. Louis Hospital, Paris. The method of treatment consisted of the boring of the lesion with a stick of metallic zinc and following this immediately with a silver nitrate stick. When he did not employ this treatment, he resorted to the Paquelin cautery.

Dr. Greenbaum said that in Brocq's clinic scarification followed by the Finsen light was largely employed.

NEO-ARSPHENAMIN DERMATITIS. Dr. Greenbaum.

F. W., a white boy, aged 10, developed a follicular eruption over the entire body after the fifth injection of neo-arsphenamin (dose 0.3 gm.). The face, as a result of scratching, had become eczematized. The itching was severe. The case was shown because of the rarity of this type of eruption complicating the administration of neo-arsphenamin.

PARAPSORIASIS. Presented by Dr. Sidlick.

A negro, aged 32, had had the disease for an indefinite time. The lesions were papular and limited to the anterior and posterior aspects of the trunk. The itching was severe. The patient also had a four plus Wassermann reaction.

DISCUSSION

Dr. Schamberg concurred in the diagnosis, but expressed the opinion that it might be a case of mycosis fungoides in its incipiency. Dr. Weidman suggested that it might be a lymphatic leukemia. Dr. Schamberg advised ultraviolet light therapy pushed to the point of producing desquamation.

ROENTGEN-RAY DERMATITIS. Presented by Dr. Dengler.

A white woman, aged 35, in 1914, received six treatments with the roentgen rays at weekly intervals, for the removal of superfluous hair on the back of both arms. The duration of each treatment was ten minutes, and the tube was about 20 inches (50.8 cm.) from the arm. About five days after the last treatment the skin became purple and the tissues speedily broke down, the arm presenting the appearance of raw meat. At the present time, both arms present ulcerative areas and scars. The arms are painful when exposed to air.

DISCUSSION

Dr. Schamberg suggested surgical removal of the involved skin and later skin grafting.

CASE FOR DIAGNOSIS. Presented by Dr. Weidman.

Sara W., colored, aged 25, said that the disease began eleven years ago, with a distribution over the shoulders. Three years ago she had a typical annular syphiloderm of the face and nodules elsewhere over the body. The Wassermann reaction was negative; however, she received thirteen injections of arsphenamin. The annular lesions disappeared, but the others remained in spite of the fact that the last nine Wassermann tests, made over a period of two years, have been negative. At present she has widely scattered pig-

mented nodules up to 1 cm. in diameter, with flat topped, translucent elevated centers; most of them are on the shoulders and the lateral aspect of the thighs. The face and arms are free. The itching is intense.

DISCUSSION

DR. SCHAMBERG suggested prurigo nodularis as the diagnosis.

Regular Meeting, Dec. 11, 1922

F. D. WEIDMAN, *Presiding*

LARVAE MIGRANS. Presented by DR. WARREN WALKER.

A boy, aged 3 years, had, on the left buttock, a narrow irregular line about 14 inches (35.56 cm.) in length and 2 mm. in width, slightly elevated and light to dark red in color. The terminals of the line showed activity, and its length was increased 2 inches (5.08 cm.) during the week it was under observation. The child had been at the seashore, and the mother thought the condition was of three months' duration.

DISCUSSION

DR. WEIDMAN said that the parasite was probably the larvae of the bot-fly. He thought it could be obtained and grown on meat.

DR. STRAUSS said that he had a case showing two narrow lines on the soles of the feet and another on the lower part of the leg. He said the cases he studied showed no eosinophilia.

RECKLINGHAUSEN'S DISEASE. Presented by DR. F. D. WEIDMAN.

Thomas C., white, 57 years old, had had the disease for twenty-seven years. This was a classical case with hundreds of cutaneous tumors and numerous freckle-like macules. The mental state was good. The patient was shown on account of associated bone changes of such a grade that Paget's disease of the bones was suspected until roentgenograms disproved any osseous thickening. They brought out marked "atheroma" of the posterior-tibial arteries, however. The legs were strongly bowed (congenital according to the patient), and the head was very large. The patient said that the changes in the skin and head had occurred after an attack of typhoid fever twenty-seven years before. The Wassermann reaction was negative; the blood counts and urinalysis were negative (eosinophils 3 per cent.); the blood urea nitrogen, 20 mg.; and chlorids, 520 mg. Sections showed a vascular fibroma containing numerous nerve trunks with medullated fibers.

EXTENSIVE TELANGIECTASIA AND PIGMENTATION (MAJOCCHI'S DISEASE). Presented by DR. JOHN H. ARNETT.

Elinor C. K., aged 25 years, white, married, said that the disease began eight years before over the right ankle, and then spread upward over the whole of the lower extremities and finally over the upper extremities. There were a few scattered points on the face and the neck. The most conspicuous

lesion was a deep, diffuse hyperpigmentation which was studded by dark freckle-like pigmentary macules. This was most marked on the ankles and legs, where the skin was also thickened and coarsely scaly. At the upper parts of the eruption only freckle-like macules were present. There were bright red punctae (some of which were comprised of several cayenne pepper-like points) both at the uppermost margins of the disease and irregularly scattered through the older parts. The condition did not quite coincide with angioma serpiginosum, Schamberg's disease, or Majocchi's disease; for an annular, serpiginous or follicular feature had not been seen. It was probably one of the many variants of the three, related more closely to Majocchi's disease. Sections showed a definite subacute to acute inflammatory process around overdistended, thrombotic capillaries, and minor hemorrhages. The following special examinations were negative: coagulation time, blood count, blood platelet count, Wassermann reaction, bacterial and protozoal stains on tissue, urinalysis. The blood pressure on two occasions was: systolic, 98, and diastolic, 74. Forcible rubbing or congestion induced by the tourniquet yielded fresh lesions, and the latter also appeared in the biopsy scar. Basal metabolism was normal.

LINGUAL TUBERCULOSIS. Presented by DR. A. STRAUSS.

F. N., a man, aged 39, born in Russia, a machinist, had a soft and hard palate almost completely covered with an elevated reddish papillomatous growth consisting of pinhead sized inflammatory papular-like lesions. Numerous minute depressions were observed in the patch, resembling the miliary abscess-like openings of the verrucous form of tuberculosis. There were various fissures, irregular in outline, over the diseased area. A few pea-sized and larger ulcers and scars from former loss of tissue were also present. There is apparently no discharge of pus or any other secretion. Cervical glands of both sides are markedly enlarged. Roentgen-ray examination of the chest showed extensive fibrocaseous tuberculosis of most of the entire right lung and the upper lobe of the left lung. Histopathologic examination of a section of the growth revealed areas of tuberculosis, although no tubercle bacilli were demonstrable. The duration of the lesion was eighteen months.

ENDOTHELIOMA CAPITIS. Presented by DR. J. B. LUDY.

Samuel D. F., aged 19 years, white, of Italian parents, about 18 months before noticed a small tumor on the right side on the supermalar region. Three months later another tumor appeared on the forehead above the right eye. During the following fifteen months a dozen more tumors appeared limited to the anterior portion of the scalp and to the right of the median line. The tumors range in size from that of a pea to that of a walnut. They were varied in shade from red to violet and were resistant though not hard as stone. During this period a small aneurysm of the artery of the right temple developed. The patient was a boxer and said that he frequently received blows on the right side of the face. The tumors bled profusely on being struck. There were no subjective symptoms.

DISCUSSION

DR. WEIDMAN concurred in the diagnosis. He said that the section was characteristic of an endothelial tumor.

CHRONIC ECZEMA. Presented by Dr. E. F. Corson.

M. G., an undersized white girl, aged 11, exhibited a generalized eczematous eruption consisting of vesicular patches with crusting and oozing, together with dry areas where marked lichenification existed. As a background there was an ichthyotic condition which had been present since the age of 18 months. The child was poorly nourished, subnormal mentally and had dry, scanty hair. With thyroid extract therapy, marked improvement had been noted during the month she had been under treatment.

John B. Ludy, Secretary.

CHICAGO DERMATOLOGICAL SOCIETY

Regular Meeting, Dec. 20, 1922.

E. A. Oliver, M.D., *Presiding*

A CASE FOR DIAGNOSIS. Presented by Dr. Stillians.

An American woman, aged 40 years, about March 1, 1922, noticed a pink, pimple-like mass in the center of her forehead. This lesion was movable, but firm in consistency; when opened it seemed to be a solid mass. The incision did not heal, but exuberant granulations grew out of it. These were removed, and the ulcer was cauterized. Large doses of roentgen ray were then employed, with only slight effect. Hemoglobin was 65 per cent.; the white blood cells numbered 10,000.

Examination revealed a rounded nodule 1 cm. in diameter, about the color of the surrounding skin, with a central shallow ulcer 0.3 cm. in diameter. The nodule was movable with the skin and not tender.

(Note: Since then a positive Wassermann reaction has been obtained. Roentgen-ray examination showed no pathologic bone condition, and no sinus could be found by probing.)

DISCUSSION

Dr. Zeisler said he thought it was a fibromatous nodule with surrounding atrophy, probably caused by roentgenotherapy.

Dr. Pusey said he thought that there was a sinus extending down to a necrotic focus, and that the only treatment was to make an incision and clean it out.

Dr. Stillians said that when the patient was first seen the lesion looked like granuloma pyogenicum, but it did not clear up under roentgenotherapy, although he gave her as much roentgen-ray treatment as he thought advisable. The lesion had been cauterized before he saw the patient. He said that he would investigate the sinus.

A CASE FOR DIAGNOSIS. Presented by Dr. Stillians.

An American, 20 years old, first noticed an eruption of large, scaly, itching patches on his chest in February, 1922. Under treatment, this condition cleared up. About October 1, another eruption appeared and had persisted since that time, fading when the patient was cold and erupting when he was warm. There was no subjective sensation. The Wassermann reaction was negative.

At presentation an eruption was seen on the chest, shoulders and abdomen, less on the neck, arms and back. The eruption consisted of small macules 1 to 3 mm. in diameter, pink, sharply defined and chiefly follicular. The lesions faded almost entirely on pressure. No scaling was present.

DISCUSSION

Dr. Pusey said that he thought it was one of the nebulous cases which it was impossible on hasty or first inspection to define.

Dr. Foerster said he could throw no light on the case. He thought the eruption was perhaps due to vasomotor instability, autotoxic in origin.

Dr. Zeisler agreed with Dr. Pusey that it was impossible to make a diagnosis on a fading eruption of this type.

Dr. Stillians said he would try to make a biopsy.

SUBCUTANEOUS SARCOID. Presented by Dr. Stillians.

A Jew, aged 21 years, a printer, in April, 1922, first noticed nodules on the left side of the chest and on the left forearm, and late in September he noticed one on the right wrist. There were no subjective symptoms, and the nodules were neither painful nor tender. The white blood count was 8,000; differential: 63 per cent. polymorphonuclears, 37 per cent. small mononuclears, 9 per cent. large mononuclears and 2 per cent. eosinophils. The Wassermann reaction was negative.

Examination revealed a rounded nodule, 15 by 0.75 cm. in diameter, over the lower rib in the left anterior axillary line, and about 2 cm. medial to this was a pea-sized, round mass, subcutaneous and not attached to the skin. On the internal surface of the upper one third of the left forearm was a similar nodule 1.5 by 1 cm., with a shot-sized mass close to it and connected with it. On the other side of the right wrist was another nodule about the size of a navy bean. The skin over these nodules was unchanged in appearance.

DISCUSSION

Dr. Senear said that he was not willing to offer a clinical diagnosis; but he thought the lesions might be lipomas rather than sarcoids.

Dr. Pusey said he thought they were benign lesions which had been present for a long time before the patient noticed them. Some were probably fibromas and some lipomas.

UNNA'S CARDLIKE SCLERODERMA. Presented by Dr. Zeisler.

A woman, aged 21 years, presented an eruption on the anterior and posterior surfaces of the neck which had been present for six months. The areas were dead white, and varied in size from that of a pin-point to that of a half dollar; they were cuboidal in shape, showing in the center some evidence of atrophy and follicular plugs.

DISCUSSION

Dr. Pusey said he believed it was a case of atrophic scleroderma occurring in patches.

Dr. Foerster concurred in the diagnosis and asked whether there was any history of injury. He said they recently had seen a patient in whom sclero-

derma followed trauma produced by a snowball being thrown against the back. The lesion appeared within a few days at about the point of trauma.

DR. ZEISLER, replying to Dr. Foerster, said there was no history of trauma, so far as he knew. He asked how frequently the small follicular plugs were present in scleroderma.

DR. PUSEY said that he believed they showed quite often when the lesions became sclerotic and flattened.

DR. SENEAR said that in the earlier literature they had formerly contended that the presence of plugs was indicative of lichen planus, but it had later been shown that they were present in both conditions.

A CASE FOR DIAGNOSIS. Presented by DR. SENEAR.

A woman, aged 18 years, in August, 1922, first noticed a scar on her right cheek. Since that time numerous other scars had developed on the cheeks and forehead. The patient said that there were no inflammatory lesions preceding the development of the scars. A moderate acne was present, but this did not involve the areas affected by the scarring. No subjective sensations were complained of. The condition corresponded closely to atrophia maculosa varioliformis cutis described by Heidingsfeld as a new disease.

DISCUSSION

DR. STILLIANS said that he had seen a similar case in a young Jewish medical student who had lesions on the left cheek, some of which were linear and much smaller than these. He thought it improbable that the girl should not know whether she had inflammatory lesions which produced the scarring, and he believed the history she gave was correct.

DR. SENEAR said he was interested in the case because he recalled that when Dr. Heidingsfeld showed his case the question was raised as to whether or not the lesions had followed acne. There was no history of acne in that case. In this girl, the acne was not in the area involved in the atrophy. The girl and her brother were both intelligent, and he was sure they were honest in their statement that there were no preliminary lesions and that she did not touch them. He had an open mind on the case but thought they could rule out any acne-like lesions preceding the atrophic areas. Heidingsfeld described a little erythema and scaling preceding his lesions, but this was not present in this case.

BROMODERMA? Presented by DR. STILLIANS.

An American youth, aged 17 years, had been run over by an automoble in August, 1922, which produced a fracture of the left foot. On the dorsum of the left foot was an area which had been excoriated and which had refused to heal, becoming raised and oozing. The area had recently decreased somewhat in size. The patient was an epileptic and had received phenobarbital (luminal), but no history of bromid medication could be obtained.

DISCUSSION

DR. PUSEY said he would not accept this as a case of bromoderma. The lesions had occurred along the site of the old injury, presumably an ulcer with granulations. He thought a more likely diagnosis was a vegetating

dermatitis. He had seen this following eczema and ulcers of the leg when there was stasis. The location and distribution were unusual for bromoderma.

Dr. Zeisler said he thought the case was a dermatitis vegetans.

Dr. Foerster said he thought it was difficult to make a differential diagnosis between bromoderma and dermatitis vegetans, as the case had the elements of both. He believed an examination of the urine to be of importance.

Dr. Senear said he was impressed with the case as a dermatitis vegetans rather than as a bromoderma.

Dr. Stillians said he had thought of dermatitis vegetans first as the lesions were crusted at that time, but there was no pus. When he heard that the patient was epileptic, he was inclined to call the condition a bromoderma, as the lesion had persisted for six months. Tests for bromin in the urine were negative.

Dr. Ravitch said he thought the condition was fungoid in origin.

A CASE FOR DIAGNOSIS. Presented by Dr. Stillians.

A man, aged 29 years, presented inflammatory lesions of the legs which had been present for a year. On healing, pigmentation and scaling occurred. There was a history of urethritis occurring after practically every intercourse and lasting for a week or two. Following these attacks, there was some joint involvement, and the lesions appeared on the legs. Several of the lesions had ulcerated, leaving scars. At presentation there was an indistinct, dark red node about the middle of the inner side of the right leg.

DISCUSSION

Dr. Foerster said he thought the condition was closely connected as to causation with vascular changes, more particularly in the veins. The patient said that he frequently had cramps in the legs at night, which together with the history of cold and clammy feet and congested, moist finger-tips, indicated a disorder of the peripheral, terminal circulation. This condition was not infrequently seen in the early stages of varicose ulcer. There was marked infiltration of the middle third of one leg, and the inner side of the left leg at its lower third showed an atrophic scarred condition due to small healed ulcerations. The picture was that of an early stage in the development of varicose ulcer.

Dr. Senear agreed with Dr. Foerster and said he thought the infiltrated leg was so much like the ones seen in varicose ulcer that he believed this was the proper explanation.

Dr. Ravitch said the patient complained first of cold feet and then of burning feet, and he said that when he was on his feet he had to stop and rest frequently. In his opinion it was a case of thrombo-angiitis obliterans.

Dr. Stillians said that he had seen the patient for the first time that day. With the history of urethritis that lasted only a short time, he thought it might be a tuberculous process, such as erythema nodosum or atypical erythema induratum which sometimes ulcerates and sometimes does not. The patient had been at the Mayo Clinic where they suspected tuberculosis of the abdomen, but operation revealed that it was normal.

GRANULOMA PYOGENICUM. Presented by Dr. Zeisler.

A boy, aged 8 years, about 1 inch below the hairline, in the middle of the posterior surface of the neck, had a flat, round, bluish-red papule about

0.75 cm. in diameter, which was apparently covered by a thin skin, which was slightly scaly. The lesion had been excised twice but recurred. There was no tenderness or itching.

DISCUSSION

DR. SENEAR said that he believed, from the extreme firmness of the lesion, that it was a vascular keloid.

DR. FOERSTER said that he agreed with Dr. Senear.

ST. LOUIS DERMATOLOGICAL SOCIETY

Regular Meeting, Jan. 10, 1923

M. F. ENGMAN, M.D., *Presiding*

A CASE FOR DIAGNOSIS. Presented by DR. R. S. WEISS.

An Italian woman, aged 38, had had a lesion on the left thigh, which, she said, began at the age of 16. There was considerable itching. She presented an oval granulomatous plaque about 4 by 6 inches (10.16 by 15.24 cm.) in size and seemingly about one-fourth inch (0.63 cm.) in thickness, apparently in the corium and situated on the left thigh just above the knee and posteriorly. At her first visit it was thought that a few satellite lesions could be made out at the periphery of the large plaque, but this feature was not so apparent at the second visit. The skin over the lesion was inflamed and somewhat lichenified.

DISCUSSION

DR. WEISS said that he was of the opinion that it was a case of chronic dermatitis with lichenification. He brought the patient to this meeting on account of the unusual depth of the thickening and its long duration.

DRS. MCINTOSH and ENGMAN said that they thought unquestionably it was a case of lichenification.

DR. R. H. DAVIS said that he thought it a case of lichenification, although judging from the sharp limitations of the lesion, one might be led to suspect that originally the trouble was a phytosis.

A CASE OF YAWS. Presented by DR. M. F. ENGMAN.

H. L. O., a colored man, aged 27, was admitted to the Barnes Hospital on Jan. 5, 1922, complaining of lesions on the face, neck, back, arms, legs, chest and abdomen, with considerable itching. The mother and father were living and well. There were six brothers, living and well; one brother was dead, cause unknown; three sisters were living and well. The patient had had measles, mumps, smallpox and whooping cough during childhood. He has been healthy since then up to the time of the present illness. He denies all venereal infections (he admits having had promiscuous sexual intercourse). He was born in Hollow Rock, Tenn., and never left that place until two years ago, at which time he moved to St. Louis. During the war, the patient was stationed at Camp Meade, Md., for two weeks. After being discharged from the army, he visited Cairo, Ill., for three months. Since his arrival in St. Louis he had worked for a packing company. His present illness began three

months ago with a small nodular lesion in front of the left ear which, the patient said, looked like a wart. This gradually increased in size, becoming harder and being covered with white scales. A physician treated him with a plaster, and the lesion became raw and bloody. He then came to the outpatient department, two months ago, for treatment, at which time the lesion was about the size of a twenty-five cent piece; it was fungating and ulcerating, and was the only lesion present. The patient also used a proprietary blood medicine, which he purchased at a drug store. Two weeks ago he noticed "pimples" on the neck, face, arms, abdomen, back and legs. These were hard, smooth and slightly elevated. They gradually increased in size and became covered with a white scale, and caused much pruritus. A lesion also developed on the roof of the hard palate. The laboratory examination revealed: 5,200,000 red blood cells, 6,600 white blood cells, and 85 per cent. of hemoglobin. The differential count was: polymorphonuclears, 62.5 per cent.; polymorphonuclear eosinophils, 1 per cent.; polymorphonuclear basophils, 1 per cent.; lymphocytes, 33 per cent.; large mononuclears and transitionals, 2.5 per cent. Prostatic Secretion: There were a few clumps of pus; the examination otherwise was negative. Urinalysis: The urine was turbid and straw-colored; the specific gravity was 1,032; acid reaction: There was a trace of albumin, no sugar was present. Microscopic Examination: A few white blood cells and epithelial cells were present and occasional hyaline casts; there were no red blood cells. The total excretion of phenolsulphonephthalein was 35 per cent. in two hours. The temperature was 37 C.; pulse rate, 84; respiration, 20. The blood pressure was: systolic, 105; diastolic, 65. The Wassermann test with cholesterin antigen was —; with noncholesterin antigen, 0. There were 30 mg. of nonprotein nitrogen per hundred cubic centimeters of blood. There were 4.2 mg. of uric acid. Dark-field examinations of serum from the lesions revealed motile spirochetes in enormous numbers, differing slightly from *Spirocheta pallida.*

Skin Lesions: The patient had a generalized eruption. The primary lesion was a nodule varying in size from 0.25 to 2 cm. These nodules occurred in groups and in circinate arrangement. When the circles of nodules contained a great many individual lesions, a plaque of granulomatous tissue was formed. The circinate lesions and the plaques were distinctly grouped. They occurred thickest over the scapular and subscapular regions, the posterior surface of the shoulders and upper arm; the lower half of the buttocks; on the external surfaces of the knee joints; on the anterior surfaces of the elbow joints; on the anterior axillary folds; on the chin, and on the forehead and neck, both anteriorly and posteriorly. The primary nodule above described was practically the same color as the skin. There was some infiltration, but not the amount found in syphilis; in fact, the lesions were somewhat elastic. The surface of many of the plaques and groups was covered with a grayish, somewhat tenacious scale. Behind the right ear and also in front and above the left ear were granulomatous, nonulcerating, healing plaques, about 3 cm. in diameter. These plaques, when the patient was first seen (two months ago), were fungating and ulcerating, and were the only lesions present. On the hard palate, just posterior to the teeth, was an ulcerated area, 2.5 cm. in diameter.

DISCUSSION

DR. ENGMAN said that this is the first case of yaws that has occurred in our clinics. It is particularly interesting in that, according to the literature on the subject, it is the only case of yaws encountered in which the patient

had not been out of the United States. This patient was born in this country and has never been away from the United States. The only suspicious source of contact was probably his stay at Camp Meade in Maryland, although he has traveled somewhat in this country.

DR. GRINDON called attention to the site of the lesion, "maman pian," as it was called in the French West Indies, that is, in front of the left ear—the next lesion, behind the right ear, occurring three weeks after the primary lesion (if the patient was not mistaken).

DR. CONRAD observed that the movement of the *Spirochaeta pertenuis* is an entirely different one from that of *Spirochaeta pallida*, being a conical movement, undulating and snakelike in character. This spirochete seemed to him thicker, and the curves somewhat deeper.

DR. ENGMAN said that one did not expect to find a spirochete (of syphilis) by dark-field examination so easily in that type of lesion, in syphilis, or so numerous, as they were in the lesions of the patient. He said that this case of yaws had been examined by Drs. Bell and Opie of Washington University, and they thought it was undoubtedly the spirochete of yaws, because of its differential points.

DR. MOOK said that he had seen a case at l'Hôpital St. Louis in Paris, exactly like the case presented, with just about as many lesions. He said that the first impression one receives is of a case of syphilis, and yet it does not look like syphilis.

DR. GRINDON remarked that the lesion at first glance resembled those of hypertrophic lichen planus.

DR. MOOK said that the condition looked somewhat like mycosis fungoides.

DR. W. D. DAVIS said that he had seen a case of yaws in Paris similar to that Dr. Mook described, and that he had also seen a case, which was undoubtedly yaws, in a negro at one of the Southern camps, Camp Beauregard, 39th Division. The patient had come into the United States from some of our island possessions, after which the lesions had spread over his body. He had fungating lesions, similar to the type that appeared on the chin of the man presented.

A CASE FOR DIAGNOSIS. Presented by DR. W. E. NETHERTON for DR. W. W. DUNCAN, Sorento, Ill.

H. B., aged 14, an American boy, had consulted Dr. Duncan because of the appearance of brown spots on the right shoulder, following exposure to sunlight when swimming. The boy had had pneumonia at the age of 7; he had had no other illnesses in childhood. The present trouble was of one year's duration. The brown spots on the shoulder gradually enlarged peripherally. He presented a large, irregular, hyperpigmented area involving the lower part of the right side of the back. This was spreading gradually peripherally. The spreading border was irregular, and near the periphery there were a few areas of normal skin which had been surrounded by the advancing borders. The surface of the lesion was smooth; there was no scaling. There was marked dermographia.

DISCUSSION

DR. DUNCAN said that he thought the lesion looked like tinea versicolor.

DR. MOOK said that he preferred to see the case several times before expressing an opinion. At first glance it looked like tinea versicolor, although

on closer inspection of the pigment in the skin, it had the appearance of lupus vulgaris; but no lupus nodules were present. He said that he thought it was very much like a nevus.

Dr. Weiss said that he thought this was merely a pigmented patch in the skin of the nevus type. If we saw such a lesion on the face of a woman, we would unhesitatingly call it chloasma.

A CASE FOR DIAGNOSIS. Presented by Dr. Conrad from Dr. Engman's clinic at Washington University.

H. F., a white boy, aged 10, presented a generalized papular eruption over the body, excluding the scalp. He had had measles, whooping cough and diphtheria at the age of 3½ years; he had had several attacks of croup and colds. His tonsils and adenoids were removed at the age of 6, after an acute purulent otitis media had cleared up. He had worn glasses during the last year. His general health had been good for the last four years. The present trouble began in June, 1922, at which time he noticed that the eyelids were reddened and tender (vernal catarrh). Four weeks before radium treatment was instituted, he had received three treatments at intervals of one week. About December 15, a red, papular eruption appeared on the neck and rapidly spread over the body. There was no itching and no constitutional symptoms. The patient said that the condition was diagnosed as "varicella" at that time. Physical examination revealed a generalized papular eruption, with here and there flat lesions and fine scales, suggestive of pityriasis rosea. On the arms and legs were crusted, pustular lesions which were thought to be suggestive of a drug eruption. They were not typical of involuting varicella lesions. A few of the papular lesions were somewhat umbilicated, but by far the majority of them were copper-hued, slightly indurated, deep-seated papules, arranged in indefinite circinate groups. The inguinal lymph nodes were enlarged, as were some of the posterior and anterior cervical nodes. The spleen was not palpable.

DISCUSSION

Dr. Engman said that he thought some of the lesions rather characteristic of pityriasis rosea with a cigaret-paper center, with a red periphery, the lesions being the size of a five-cent piece, whereas the entire body was studded with distinct papular lesions of a copper tint, which were rather infiltrated, but not as hard as those of syphilis. The skin had also a swollen, red appearance, which may accompany any acute eruption. Some of the lesions were crusted from scratching and quite papular, while others had the appearance of pityriasis rosea.

Dr. Grindon said that he thought the wide flat papules in circumscribed patches at first gave the appearance of an acute lichen planus; but otherwise they did not resemble this condition.

Dr. W. D. Davis said that in his opinion the case was a papular type of pityriasis rosea, and that the lesions on the back in the lumbar region and along the flank were more or less suggestive of the plaque type of pityriasis rosea. The fact that some of the lesions were crusted and papular indicated that the eruption was pruritic. The fact also that the lesions were on the face made this an unusual and most interesting type of the disease.

Dr. R. H. Davis said he thought it looked like pityriasis rosea.

Dr. Mook said that he saw the patient when the condition began several weeks ago. The boy came to his office for treatment of vernal conjunctivitis.

Radium was applied to the eyelids. Shortly after, the mother said: "He has 'skin spots.'" The chest and neck were examined, revealing six or eight vesicopapules scattered over the neck, chest and back. The mother was told that the boy had chickenpox; this was three weeks ago. That was the last time the boy was observed until today. Dr. Mook said that from certain characteristics not previously noted, he thought the lesions looked like pityriasis rosea, atypical pityriasis rosea of the papular type with vesiculation.

DR. TOBIAS inquired whether this patient had any constitutional symptoms.

DR. MOOK replied that he had not.

DR. WEISS said that he had seen the patient several times since he first came to the clinic. The boy had a number of plaques varying in size from 0.25 to 2 cm., which were typical of pityriasis rosea. In addition, scattered over the arms was a large number of papular lesions that appeared to be more like a drug rash than pityriasis rosea. At the time of the third visit, some of the plaques had involuted to such an extent that they did not appear to be quite so much like the plaques of typical pityriasis rosea. We have seen vesicles in pityriasis rosea before, and for this reason we did not exclude the diagnosis. The occurrence of other lesions is suggestive of a drug eruption. A few of the lesions were pustular and appeared like those of iodid. However, Dr. Weiss said that he believed this case to be that unusual type of pityriasis rosea which we see occasionally, especially in children.

DR. ENGMAN said that he thought the case was most interesting. When he first saw it (two days before) he thought it was varicella. Now, however, some of the lesions looked more characteristic of pityriasis rosea. Some on the chest were typical of pityriasis rosea with a cigaret-paper center, spreading peripherally and clearing up somewhat in the center. From observations made in St. Louis on cases of pityriasis rosea, Dr. Engman said he felt that the dermatologist should be careful to differentiate between the various types mentioned in this discussion. Several days ago he had a patient who in the first few days showed a large number of papules with lesions distributed over the face and neck which in a few days showed characteristics of typical pityriasis rosea. The case under discussion, Dr. Engman observed, looked more like pityriasis rosea than any other lesion mentioned.

DR. CONRAD said he thought at first that it was a case of pityriasis rosea, but on further inspection, owing to the color and circinate character of the lesions, with some infiltration of those lesions on the limbs, he thought it looked almost like typical secondary lesions. A Wassermann test gave negative results, however, and he decided that it was a pityriasis rosea of a papular type.

A CASE FOR DIAGNOSIS. Presented by DR. TOBIAS.

Mrs. E. T., aged 45, a waitress, presented herself at the Dermatological Clinic of the Barnard Free Skin and Cancer Hospital, with a lesion on the right leg of six months' duration. She now presented a large, chronic, moderately infiltrated, scaly patch, involving the lower third of the leg, extending upward from the ankle and involving the entire anterior and lateral aspects of the limb. The upper border of the lesions was peculiar in that it was serpiginous and the seat of inflammatory activity. The condition was gradually spreading upward. There were no subjective symptoms. The Wassermann test was positive.

DISCUSSION

DR. ENGMAN said that this case was a type of chronic eczematoid dermatitis, one of the types that he had described in 1902, a dermatitis characterized by similar lesions on the leg. He said that many years ago he had seen good results following the use of 5 per cent. pulverized rhubarb in petrolatum for such conditions on the leg. Rhubarb contains a small percentage of chrysarobin, which is sometimes used for such conditions.

A CASE FOR DIAGNOSIS. Presented by DR. TOBIAS.

Mrs. R. W., aged 58, a domestic, entered the dermatologic clinic of the Barnard Free Skin and Cancer Hospital, presenting an oval, well-defined, chronic, moderately infiltrated scaly plaque on the scalp in the right parietal region, of one year's duration, beginning as a pruritic erythematous area, which the patient scratched. On removal of the thick scales, a red, weeping surface was disclosed. The hairs were not involved. The Wassermann report was not available.

DISCUSSION

DR. GRINDON said that occasionally this condition is seen on the temple, and sometimes just within the hairline of the forehead; again, on the chin. In his opinion it is quite the same thing as Paget's disease. He had seen the condition about the scrotum, also extending over the thorax.

DR. ENGMAN said that he concurred in this opinion of Dr. Grindon. He thought it a valuable observation to keep in mind in the dermatologic clinics, where there are a large number of so-called malignant conditions of the skin to deal with. He said that he had insisted in the Barnard Free Skin and Cancer Hospital clinic that these peculiar conditions, such as presented by Dr. Netherton, be called "malignant papillary dermatitis," after Fordyce, or "extramammary Paget's disease." Extramammary Paget's disease is overlooked and is classified under various names, such as Bowen's disease, which is, he believes, a type of Paget's disease and should be classified as extramammary Paget's disease. Many cases have been observed; in the course of time all develop markedly malignant symptoms, and their characteristics as such are indistinguishable from that type discussed by Bowen.

DR. GRINDON asked Dr. Engman whether he believed any stage of this disease could be called precancerous.

DR. ENGMAN replied that it could not be called precancerous, that always, from the beginning, it was cancer.

DR. ENGMAN replied that it could not be called precancerous; that always or chronic dermatitis, and is followed later by a true tumor in the gland tissue. The histology of the tumor is distinctly different from that of the skin condition, which shows hyperplasia with vacuolation of the cells. The tumor itself shows true carcinoma, which is entirely different from the histologic appearance of the skin. This case might be mentioned under the classification of mammary rodent ulcer type, which is a distinctly different kind of tumor from that which occurs in carcinoma of the breast itself. In other words, Paget's disease skin histology is distinctly different from tumor histology. There was a case in the Barnard Free Skin and Cancer Hospital of a woman who had numerous patches of eczematoid lesions, in the center of which grew large carcinomas, true carcinomatous tumors, as large as a walnut, while this is a flattened lesion that grows more like a rodent ulcer type.

DR. ENGMAN remarked that he thought this whole question could be likened to that of mycosis fungoides. It is mycosis fungoides from the beginning, and not eczema. The histopathology of so-called Paget's disease and Bowen's precancerous glands is entirely different from that of rodent ulcer pathology in the appearance and arrangement of the chromatin about the nucleus, a chromatin arrangement which marks them as malignant cells. They are malignant from the beginning, and the difference in histology is due to the difference in location. Premammary Paget's disease occurs on the vulva or the penis. True carcinoma-like lesions of the glands appear later. We have seen malignant papular dermatitis of the penis which in the course of some months would develop true characteristic carcinoma with metastasis in other portions of the body. The lesions in the beginning are eczema-like in appearance. Yet they are carcinomatous from the very beginning, as shown in pathologic study. Most authors agree today that so-called Paget's disease is cancer from the very first symptoms of the dermatitis, and it is not a dermatitis but a dermatitis-like lesion containing malignant cells which metastasize into the breast and cause the obvious characteristics of carcinoma.

DR. GRINDON said that it was his belief that the discussions in the textbooks to the effect that this condition begins in an eczema or eczema-like dermatitis were written by surgeons, not by trained dermatologists; he had never seen a case of Paget's disease which looked like an eczema on close inspection. He suggested that the term eczema-like lesions should be corrected.

VIENNA DERMATOLOGICAL SOCIETY

Session of Feb. 9, 1922

DR. NOBL, *Presiding*

ULCUS PHAGEDENICUM CRURIS. Presented by DR. BRÜNNAUER.

In the case presented, that of a woman, there was an ulcer on the leg, the size of a dollar. The edges of the lesion were undermined, soft and slightly suppurating. The Wassermann reaction and luetin test were negative. Application of hydrogen peroxid quickly flattened the lesions and improved the condition. In the discussion, Fischel stated that, in two cases of phagedenic ulcer, he had found tetanus-like bacilli. These were also found in the case presented. Histologic details could not yet be given.

LUPUS VULGARIS LIMITED TO THE HAIRY SCALP. Presented by DR. KUMER.

A man had suffered trauma of the head twenty years previous to the development of the present disorder.

ERYTHEMA EXUDATIVUM MULTIFORME. Presented by DR. ARZT.

In a woman of 47, fever and pains in the joints were followed by development of polymorphic exanthems on the back of the hands, arms and cheeks. There were numerous disseminated, light red and partly bluish eruptions all over the body. Some lesions were hemorrhagic.

Session of Feb. 23, 1922

PSORIASIS ON A SEBORRHEIC BASIS. Presented by Dr. Reiner.

There was a bluish red exanthem covering the trunk and extremities, forming irregularly defined patches with a slight, pityriasiform scaling. The extremities also showed hemispheric nodules, rising above the skin surface and carrying a tender whitish scale on their summit. Diagnosis was difficult, as sites of predilection were not affected. Parapsoriasis was a possibility.

SENILE KERATOMA WITH TRANSITION INTO EPITHELIOMA. Presented by Dr. Brünnauer.

The skin of the face of a patient, aged 84, was tough, dry and wrinkled, with symptoms of a senile degeneration. The seborrheic skin of parts of the face carried flat wartlike formations (verrucae seborrheicae seniles). One of these developed into an epithelioma, causing destruction of tissue around the right ear. Senile keratoma is rather frequent in peasants who are exposed to the sun, degeneration into epithelioma, however, being relatively rare.

STOMATITIS ULCEROSA MERCURIALIS FOLLOWING AMMONIATED MERCURY OINTMENT. Presented by Dr. Riehl.

A patient with psoriasis had been treated with ammoniated mercury and then lenigallol. In a test tube, an alkaline solution of lenigallol mixed with ammoniated mercury caused a gray-green deposit of finely distributed (colloidal) mercury.

Session of March 9, 1922

ERYTHEMA TOXICUM IN WIDESPREAD SCABIES PUSTULOSA AND IMPETIGO CORPORIS. Presented by Dr. Krüger.

A girl of 5, in addition to serious scabies pustulosa developed toxic erythema consisting of numerous pea-sized sharply defined eruptions, which disappeared on pressure.

SECONDARY SYPHILIS WITH SYPHILITIC PHLEBITIS. Presented by Dr. Unterkircher.

Phlebitic nodules developed on the leg of a woman, aged 29, with disappearing secondary symptoms.

LIVEDO RACEMOSA IN SYPHILIS. Presented by Dr. Ehrmann.

A patient with a positive Wassermann reaction developed on the skin of the back, breast and upper and lower extremities the typical branched drawings with an hyperemic, more elevated main-branch with thinner side branches.

TUBERCULOSIS ULCEROSA ANI. Presented by Dr. Arzt.

A case was presented in which there were typical nodules, yielding tubercle bacilli.

PURPURA. Presented by Dr. Randak.

A woman, aged 62, suffered from nasal hemorrhages followed by hemorrhages into the skin of the extremities. The mucosa of the mouth and of the bladder was also affected. The blood picture revealed: 5,000,000 erythrocytes and 6,800 white cells, of which 50 per cent. were neutrophils, 2 per cent. eosinophils, 5 per cent. mast cells and 43 per cent. lymphocytes, with scarcely any blood platelets.

SECONDARY SYPHILIS WITH TOPHI, ARTHRITIS, OSTEOPERIOSTITIS AND TENDOVAGINITIS. Presented by Dr. Unterkircher.

A woman, aged 22, with secondary syphilis developed tophi and osteoperiostitis on the right os carpale. There was also hygroma, which pointed to a syphilitic tendovaginitis simplex.

ICHTHYOSIS IN AN UNUSUAL LOCATION. Dr. Riehl.

The lesions were sharply defined and limited to the sole of the foot.

TUBERCULOSIS ULCEROSA LINGUAE. Dr. Arzt.

There were extensive ulcerations under the left side of the tongue in a man with apical tuberculosis. Histologically, there were epithelioid cell tubercles and giant cells. Tests for tubercle bacilli were positive.

FAVUS CORPORIS. Dr. Fuhs.

A dollar sized lesion with several sulphur-yellow scutula developed on the leg of a girl. The source of infection was unknown.

Session of March 23, 1922

ERYTHEMA MULTIFORME WITH INVOLVEMENT OF THE BUCCAL MUCOSA AND CONJUNCTIVA. Presented by Dr. Arzt.

The patient had had a relapse every spring during the last six years. There were macular, papular and vesicular eruptions on the inner side of the left cheek and on the conjunctiva of the left eye.

ERYTHEMA MULTIFORME WITH LARGE NODULES. Dr. Arzt.

Histologic investigation showed that the inflammation was not syphilitic.

SCLEROSES. Dr. Hofmann.

The patient had an initial sore on the lower lip and swelling of the submaxiliary glands concomitant with a typical initial sore of the glans penis and swelling of the inguinal glands.

UNUSUAL EPITHELIAL DERMATOSIS WITH EXTENSIVE ABSCESS FORMATION. Drs. Planner and Strassberg.

Clinically, this disorder showed an exanthem of small superficial nodules with a yellowish brown central scale. There were also extensive furuncle-like

abscesses almost palm size. Histologically, the disorder begins with a broad proliferation of the epidermis into the corium and a subsequent central parakeratotic cornification. Secondarily, *Staphylococcus pyogenes-aureus* invades the cornification, destroying the epithelial basis of the proliferation and penetrating to the collagenous tissue. This disorder, therefore, represents an epitheliosis which is secondarily infected with staphylococci, and which clinically resembles acne and its complications.

ASPHALT DERMATITIS. Dr. Fischl.

Three workmen handling asphalt developed a serious dermatitis of the face, with scaling, deep pigmentation and hyperkeratosis. Clinically and etiologically, the disorder resembled the petrolatum dermatitis described by Oppenheim.

ERYTHRODERMA EXFOLIATIVA RECIDIVANS FOLLOWING ADMINISTRATION OF NEO-ARSPHENAMIN. Dr. Oppenheim.

This case belongs to that group of cases of arsenic intoxication which are marked by relapsing erythemas and exfoliation, loss of hair and nails, presence of arsenic in the urine and the corneous substances and involvement of the mucosa and kidneys. This disorder must be differentiated from the erythema which develops immediately after an injection and which constitutes an idiosyncrasy to arsphenamin; it must also be differentiated from the "fixed" arsphenamin erythemas, as well as from the urticarial and eczema-like eruptions.

BERLIN DERMATOLOGICAL SOCIETY

Session of Feb. 14, 1922

CARCINOMA DUE TO ROENTGEN RAYS FOLLOWING IRRADIATION OF PSORIASIS LESIONS ON THE HANDS. Presented by Dr. Halberstädter.

Carcinoma developed four years after several series of exposures to the roentgen ray. Radium was tried. In the discussion Dr. Blumenthal warned against repeatedly irradiating in relapses of psoriasis.

CONGENITAL SYMMETRICAL PROGRESSIVE ERYTHROKERATODERMA. Presented by Dr. Gottron.

The patient presented had sharply defined hyperkeratotic lesions on the ears, chin, elbows, hands, etc. The lesions had a brownish red outline. Diagnostically, psoriasis vulgaris and pityriasis rubra pilaris must be excluded. The picture presented is rare. In the discussion, Dr. Pulvermacher stated that a case of érythrodermie ichthyosiforme congénitale presented in 1919 showed all the symptoms of the foregoing disorder. These cases belong to the neviform group (the genodermatoses Meirowsky and genoderma Bettmann).

PEMPHIGUS SERPIGINOSUS. Presented by Dr. Gottron.

In the discussion of this case, which was held to be a dermatitis herpetiformis, it was proposed to apply Jadassohn's provocation method with potassium iodid, to secure a definite diagnosis.

Session of May 9, 1922

EXPERIMENTAL THALLIUM ALOPECIA. Dr. Buschke.

Injections of thallium into rats caused complete alopecia. An endocrine disturbance is assumed. Thallium is considered an endocrine poison par excellence. Buschke's experiments confirm the assumption that the whole endocrine system is one uniform organ.

SYPHILIS OF THE PAROTID. Dr. Sklarz.

Swelling of left parotid gland, syphilitic alopecia, leukoderma and a positive Wassermann reaction were present. Inunction treatment and iodin effected regression of the parotitis.

LUPUS AND TERTIARY SYPHILIS. Dr. Ledermann.

In a patient who had suffered from lupus since childhood, there developed warty, crusty lesions, which were held to be lupus tumidus. A four plus Wassermann test, however, and regression of nodules, as well as cessation of suppuration after inunction treatment, pointed to tertiary syphilis.

A CASE FOR DIAGNOSIS. Dr. W. Fischer.

The patient had an exanthem which consisted of urticaria-like wheals and also of obstinate hard eruptions, shiny and of a yellowish shade. Histologically, there were only superficial inflammatory changes. The disorder probably belongs to the group of urticaria perstans.

FAVUS ON THE BACK OF THE HAND CAUSED BY INFECTION FROM A CANARY. Dr. Fischer.

The diseased animal showed distinct scutula formation on the head. In the discussion, Heller stated that he had found favus in the nightingale and the lark.

Session of June 20, 1922

WHAT IS THE SPECIFIC EFFECT OF MERCURY IN THE TREATMENT OF SYPHILIS? Dr. Schumacher.

The effect of mercury is due to a catalytic hastening of the oxidating and metabolizing processes in the cell by the free mercury ions. Mercury has no spirillicidal effect. Schumacher believes that the comparatively good dissociation of the mercury-serum compound, the lack of nucleic acid in *Spirochaeta pallida*, as well as the abundance of nucleic acid cells in a syphilitic tissue, account for the specific effect of mercury. Therapeutically, inunction treatment is most effective. Syphilitic patients treated with mercury tend to lose

weight, owing to the increased oxidation process, while patients treated with arsenic gain weight, as arsenic which is a catalyzator poison impedes oxidation processes. Arsphenamin medication should be followed by treatment with mercury.

PIGMENTATION FOLLOWING DERMATITIS EXFOLIATIVA. Dr. Buschke.

A case of dermatitis exfoliativa with rise in temperature and serious constitutional involvement was followed by extensive development of dark brown pigmentation. A disturbance in the vegetative nervous system was assumed to be the causative factor.

AN UNUSUAL EXANTHEM FOLLOWING ENERGETIC ARSPHENAMIN MEDICATION. Dr. Buschke.

Eruptions resembling monorecurrences occurred in a patient with syphilis who had received sixty-five injections of arsphenamin within three years. Buschke believes that the spirochetes had become arsphenamin-fast and that their virulence had thus been increased.

AN UNUSUAL CASE OF DARIER'S DISEASE. Dr. Arndt.

The lesions were located unilaterally within the second to seventh intercostal space.

ACQUIRED ESSENTIAL MULTIPLE TELANGIECTASIS. Dr. Arndt.

Telangiectasis symmetrically located on the lower extremities developed within three years in a patient aged 35. The patient had a goiter, but it was not exophthalmic.

DERMATITIS FOLLOWING ORAL ADMINISTRATION OF CALOMEL. Dr. Gottron.

A patient was given two 0.2 gm. tablets of calomel a week, for five consecutive weeks, for constipation. Erythema and stomatitis developed followed by a serious exfoliative erythroderma, which has now persisted for months.

ARSPHENAMIN RESISTANT CASES OF SYPHILIS. Dr. Heyn.

A patient with seropositive primary syphilis developed an unusual exanthem and serious constitutional disturbances in spite of energetic arsphenamin and mercuric salicylate treatment. Inunction treatment caused rapid improvement. In another case of primary syphilis, combined treatment with mercury and arsphenamin was followed by the development of palm-sized infiltrations and pustular eruptions. These lesions also quickly cleared up under inunction treatment. These arsphenamin resistant cases are comparatively frequent. While the Wassermann reaction is often negative, the general constitutional involvement may be serious.

KERATOSIS FOLLICULARIS FOLLOWING ARSENIC MEDICATION. Dr. Bruhns.

A typical keratosis follicularis developed in an arsenic dermatosis. The lesions developed on areas which had not been affected previously. The condition was considered as an arsenic keratosis.

MUNICH DERMATOLOGICAL SOCIETY

Session of Feb. 24, 1922

A CASE OF ACRODERMATITIS CHRONICA ATROPHICANS IN A LABORER, AGED 62. Presented by Dr. Thieme.

The patient had a case of untreated syphilis without symptoms, and with acrodermatitis lesions on the backs of the hands, on the forearms and on both legs. Prolonged exposure to cold and damp air was assumed to be cause of disorder.

A NEW TYPE OF SKIN DISEASE RESEMBLING THE KERATOSIS FOLLICULARIS OF BROOKE. Dr. Siemens.

Dr. Siemens observed a cornification anomaly in mother and son. The lesions represented a comedo-like, acneform follicular keratosis of varying intensity along the extensor sides. The disorder differs from Brooke's keratosis in that it is of congenital nature, prefers the extensor surfaces, particularly the knees and elbows, and is combined with alterations of the nails, keratosis of the mucosa and plantar keratosis. The disorder could not be influenced therapeutically.

Session of March 24, 1922

ACRODERMATITIS ATROPHICANS WITH ERYTHROMELIA (PICK'S SYNDROME). Presented by Dr. Tiefenbrunner.

The patient had edematous swelling of both legs and extensive atrophy of the skin on the elbows, knees and backs of the feet. The skin on these sites was a violet red. Prolonged exposure to cold air was assumed as a possible etiologic factor.

HISTOLOGIC EXAMINATION OF ACRODERMATITIS CHRONICA ATROPHICANS. Dr. Poehlmann.

Sections were demonstrated showing the various stages of acrodermatitis. The microscopic picture of the inflammatory swelling stage of acrodermatitis showed great dilatation of the vessels, small-cell infiltration of the collagenous tissue, lack of elastin in the papillary body. Proliferation of the endothelium in the capillaries was pronounced. The etiology of acrodermatitis is unknown. In the discussion, the chronic inflammation was considered the primary and important characteristic of this disorder, as the atrophy develops secondarily sooner or later. Hence it follows that an idiopathic atrophy of the skin—strictly speaking—does not exist.

Session of May 26, 1922

TECHNICAL IMPROVEMENTS IN PROPHYLAXIS. Dr. Lenz.

A 0.3 per cent. mercuric chlorid ointment is advised as a prophylactic for gonorrheal and syphilitic infections. This ointment should not be kept in

metal tubes, as mercuric chlorid (corrosive sublimate) is reduced to mild mercurous chlorid (calomel). The product of Dr. Lenz is hydrous wool fat containing 0.3 per cent. mercuric chlorid in a water and airproof parchment bag.

A CASE OF URTICARIA PERSTANS WITH PIGMENTATION. Dr. Siemens.

The patient had a wheal on the elbow and on the neck. There was a spot of pigment with localized urticaria factitia on the left thigh.

TENTH SESSION OF THE NORTHWEST GERMAN DERMATOLOGICAL SOCIETY

Session of March 26, 1922

Dr. Stümpke, *in the Chair*

A CASE OF UNEVEN THINNING OF THE HAIR. Presented by Dr. Riecke.

The long hair of the scalp of a girl, aged 8, appeared to be twisted at regular intervals, thus appearing thinner in these parts. It was not a case of pili monileformes. Dr. Riecke suggested the name "trichokinesis" for this disorder.

NEURINOMATOSIS. Dr. Schmitt.

In his most recent investigations concerning neurinomatosis, Meirowsky traces the "vitium primae formationis" of this disorder back to the germ-plasm.

MACROCHEILIA. Dr. Schütz.

Diagnostically, Dr. Schütz differentiates this condition from scrofulosis, hemangioma and lymphangioma. Histologic investigation revealed, besides thickening of the epithelium, a distinct dilatation of the blood and lymph spaces, as well as destructive alterations and degeneration of the elastic fibrils. Therapeutic measures were ineffective.

INITIAL SORE ON THE LEFT SIDE OF OCCIPUT. Dr. Stümpke.

A man, aged 32, had a sharply defined lesion, the size of a fist. The patient said that he had been bitten during a wrestling match.

ROENTGEN-RAY ULCER. Dr. Stümpke.

The ulcer was healed by exposure to the Alpine sun lamp (10 cm.) and irrigation with potassium permanganate.

LUPUS ERYTHEMATOSUS. Dr. Stümpke.

This disease was present in a woman, aged 30. Compression treatment with the Kromayer quarz lamp caused rapid improvement.

SILESIAN DERMATOLOGICAL SOCIETY

Session of May 6, 1922

MERCURIC CHLORID NECROSIS OF THE URETHRAL MUCOSA. Dr. Vogel.

Injection of a 5 per cent. mercuric chlorid solution into the urethra caused nerosis of the mucosa, colic, diarrhea with hemorrhage, anemia and foul breath.

ERYTHEMA INDURATUM (BAZIN) AND PAPULONECROTIC TUBERCULID. Dr. Wiener.

The patient had typical acnitis nodules on the knees and elbows; there were also erythema induratum lesions. The Pirquet reaction was positive. In the discussion, Jadassohn said that this form of erythema induratum represents an intermediate stage of development into a subcutaneous sarcoid.

A TYPICAL TUBERCULOSIS OF THE SKIN. Dr. Hoffmann.

A man, aged 73, developed palm-sized, sharply defined lesions on both sides of the neck. The lesions consisted chiefly of dark gray, wartlike elevations covered with hard corneous material. The Pirquet reaction was positive. Histologic investigation revealed inflamed tuberculous tissue and giant cells. Tubercle bacilli were found in the granulation tissue. In the discussion, Jadassohn pointed to the typical course of some cases of senile tuberculosis cutis which resemble the serpiginous-fungus forms previously described by him.

KELOID. Dr. Martenstein.

The patient had extensive keloid resulting from a burn. This was successfully treated with deep roentgen-ray irradiation. In the discussion, it was advised to irradiate only fresh keloids. Old thick scars yield better to mesothorium. This is best applied to that part of scar which is thickest and causes most tension. The cosmetic result will be better than by exposing the whole scar in its entire length.

LUPUS VULGARIS PAPILLOMATOSUS AURICULI. Dr. Martenstein.

The patient had small papillomatous lesions on the ear. These proliferations were not secondary symptoms, but microscopically were found to consist of tuberculous tissue. Lesions of this kind have seldom been seen on the ear.

A CASE OF SECONDARY AND TERTIARY SYPHILIS. Dr. Freudenthal.

A woman who had received a strenuous course of treatment with mercury and arsphenamin shortly after infection two years ago, within a few days developed an exanthem which was remarkable for its symmetrical location along both extremities, the papular character of the eruptions and their serpiginous spreading.

LICHEN SCROFULOSUS WITH TRANSITION INTO PAPULONECROTIC TUBERCULIDS. Dr. Freudenthal.

A child, aged 8, showed scars of lichen scrofulosus on the knees and papulopustular tuberculids on the arms. The Pirquet reaction was positive as was also the reaction to 25 per cent. Moro ointment. Histologically, a pustule showed inflammatory symptoms on the surface and had a pronounced tuberculoid structure.

CULTIVATION OF FUNGI FROM THE BLOOD IN DEEP TRICHOPHYTINA WITHOUT LICHEN TRICHOPHYTICUS. Dr. Jessner.

The following experiment shows that in deep trichophytina fungi may be found to circulate in the blood which carries them into the skin. In a case of deep trichophytina of the beard, injections of trichophytin vaccine were made into the lesions as well as intravenously, in order to cause lichen trichophyticus. This was not possible, yet a gypseum fungus was obtained from both the blood and the beard. A lichen disease did not develop because either fungi do not locate in the skin but pass the capillaries and perish in the blood, or the degree of skin allergy is not suitable for a reaction with the fungi.

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